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FIG.1A

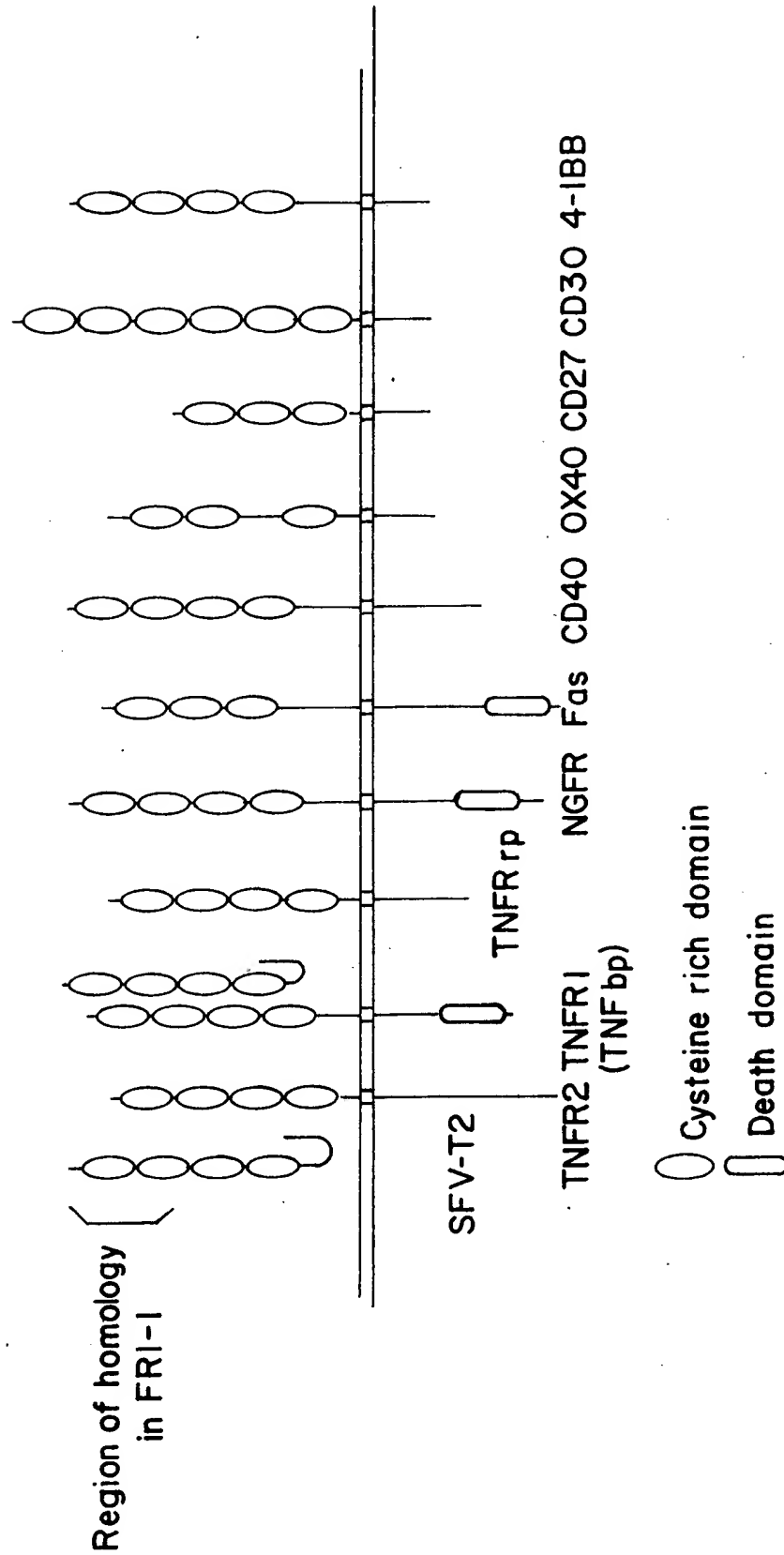
	148	178	208	238	268	298
FRI-1	ALLVFLDIIIEWTTQETFPFKYLHYDPETGRQLLCDKCAPGTYLKQHC.TVRRKTLCV.PCPDY.SYTDSCD					
				:	:	:
SW: TNR2_HUMAN	30	40	50	60	70	80
	HALPAQVAFTPYAPEGSTCRLREYYDQTAQMCCSKCSPGQHAKVFCTKTSDTVCDSCD					
	328					
FRI-1	YSYTDSWHTS					
	: : : :					
SW: TNR2_HUMAN	90	100	110	120	130	140
	STYTQLWNWVPECLSCGSRCSDDQVETQACTREQNRICTCRPGWCALSKQEGCRLCAPL					

FIG.1B

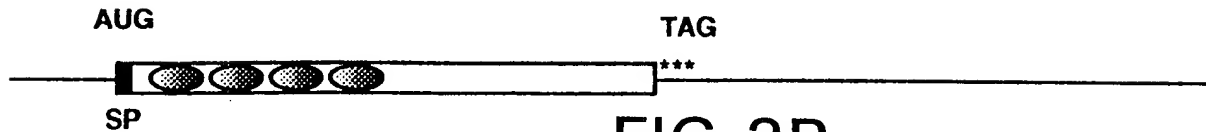
FRI-1	69	YLHYDPETGRQLLCDKCAPGTYLKQHC.TVRRKTLCV.PCPDY.SYTDSCD
		. . . .   .       :   .   :     :   .   .
TNFR profile	6	YHYDQNGRMCECHMCQPGHFLVKHCKQPKRDTVCHKPCPEPGVTYTDW
FRI-1	116	H
TNFR profile	56	H

Z Score = 8.29

FIG. 1C



## FIG.2A



## FIG.2B

10 30 50  
ATCAAAGGCAGGGCATACTTCCTGTTGCCAGACCTTATATAAAACGTCATGTTTCGCCTG  
70 90 110  
GGCAGCAGAGAAGCACCTAGCACTGGCCCAGCGGCTGCCGCCTGAGGTTTCCAGAGGACC  
130 150 170  
ACAATGAACAAGTGGCTGTGCTGTGCACTCCTGGTGTCTTGGACATCATTGAATGGACA  
M N K W L C C A L L V F L D I I E W T  
190 210 230  
ACCCAGGAAACCTTTCCTCCAAAATACTTGCATTATGACCCAGAAACCGGACGTCAGCTC  
T Q E T F P P K Y L H Y D P E T G R Q L  
250 270 290  
TTGTGTGACAAATGTGCTCCTGGCACCTACCTAAAACAGCACTGCACAGTCAGGAGGAAG  
L C D K C A P G T Y L K Q H C T V R R K  
310 330 350  
ACACTGTGTGTCCCTTGCCCTGACTACTCTTATACAGACAGCTGGCACACGAGTGATGAA  
T L C V P C P D Y S Y T D S W H T S D E  
370 390 410  
TGCGTGTACTGCAGCCCCGTGTGCAAGGAAGTGCAGACCGTGAAACAGGAGTGCAACCGC  
C V Y C S P V C K E L Q T V K Q E C N R  
430 450 470  
ACCCACAACCGAGTGTGCGAATGTGAGGAAGGGCGCTACCTGGAGCTCGAATTCTGCTTG  
T H N R V C E C E E G R Y L E L E F C L  
490 510 530  
AAGCACCGGAGCTGTCCCCCAGGCTTGGGTGTGCTGCAGGCTGGGACCCAGAGCGAAAC  
K H R S C P P G L G V L Q A G T P E R N  
550 570 590  
ACGGTTTGCAAAAGATGTCCGGATGGGTTCTTCTCAGGTGAGACGTCATCGAAAGCACCC  
T V C K R C P D G F F S G E T S S K A P  
610 630 650  
TGTAGGAAACACACCAACTGCAGCTCACTTGGCCTCCTGCTAATTCAGAAAGGAAATGCA  
C R K H T N C S S L G L L L I Q K G N A  
670 690 710  
ACACATGACAATGTATGTTCCGGAACAGAGAAGCAACTCAAATTTGTGGAATAGATGTC  
T H D N V C S G N R E A T Q N C G I D V  
730 750 770  
ACCCTGTGCGAAGAGGCATTCTTCAGGTTTGTGCTGTGCCTACCAAGATTATACCGAATTGG  
T L C E E A F F R F A V P T K I I P N W  
790 810 830  
CTGAGTGTTCTGGTGGACAGTTTGCCTGGGACCAAAGTGAATGCAGAGAGTGTAGAGAGG  
L S V L V D S L P G T K V N A E S V E R  
850 870 890  
ATAAAACGGAGACACAGCTCGCAAGAGCAAACCTTTCCAGCTACTTAAGCTGTGGAAGCAT  
I K R R H S S Q E Q T F Q L L K L W K H  
910 930 950  
CAAAACAGAGACCAGGAAATGGTGAAGAAGATCATCCAAGACATTGACCTCTGTGAAAGC  
Q N R D Q E M V K K I I Q D I D L C E S  
970 990 1010  
AGTGTGCAACGGCATATCGGCCACGCGAACCTCACCACAGAGCAGCTCCGCATCTTGATG  
S V Q R H I G H A N L T T E Q L R I L M

## FIG. 2C

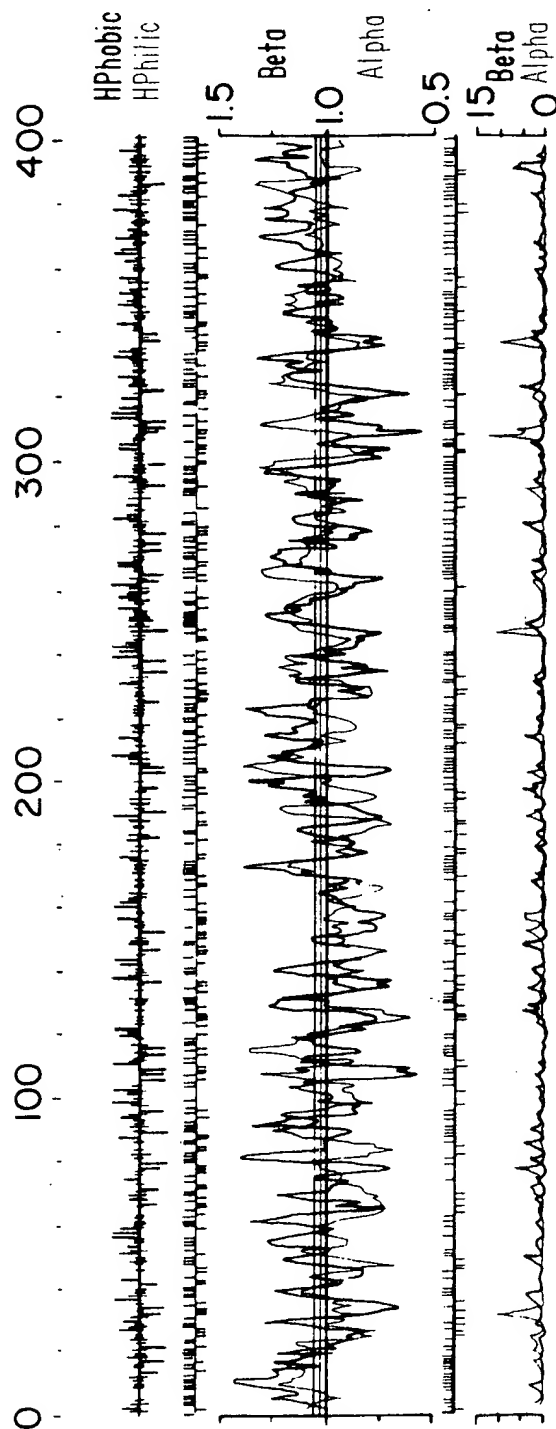
1030 1050 1070  
GAGAGCTTGCCTGGGAAGAAGATCAGCCCAGACGAGATTGAGAGAACGAGAAAGACCTGC  
E S L P G K K I S P D E I E R T R K T C  
1090 1110 1130  
AAACCCAGCGAGCAGCTCCTGAAGCTACTGAGCTTGTGGAGGATCAAAAATGGAGACCAA  
K P S E Q L L K L L S L W R I K N G D Q  
1150 1170 1190  
GACACCTTGAAGGGCCTGATGTACGCACTCAAGCACTTGAAAGCATACCACTTTCCCAAA  
D T L K G L M Y A L K H L K A Y H F P K  
1210 1230 1250  
ACCGTCACCCACAGTCTGAGGAAGACCATCAGGTTCTTGACAGCTTCACCATGTACCGA  
T V T H S L R K T I R F L H S F T M Y R  
1270 1290 1310  
TTGTATCAGAAACTCTTTCTAGAAATGATAGGGAATCAGGTTCAATCAGTGAAGATAAGC  
L Y Q K L F L E M I G N Q V Q S V K I S  
1330 1350 1370  
TGCTTATAGTTAGGAATGGTCACTGGGCTGTTTCTTCAGGATGGGCCAACACTGATGGAG  
C L  
1390 1410 1430  
CAGATGGCTGCTTCTCCGGCTCTTGAAATGGCAGTTGATTCCTTTCTCATCAGTTGGTGG  
1450 1470 1490  
GAATGAAGATCCTCCAGCCCAACACACACACTGGGGAGTCTGAGTCAGGAGAGTGAGGCA  
1510 1530 1550  
GGCTATTTGATAATTGTGCAAAGCTGCCAGGTGTACACCTAGAAAGTCAAGCACCCCTGAG  
1570 1590 1610  
AAAGAGGATATTTTTATAACCTCAAACATAGGCCCTTTCCTTCCTCTCCTTATGGATGAG  
1630 1650 1670  
TACTCAGAAGGCTTCTACTATCTTCTGTGTCATCCCTAGATGAAGGCCTCTTTTATTTAT  
1690 1710 1730  
TTTTTTATTCTTTTTTTTCGGAGCTGGGGACCGAACCCAGGGCCTTGCGCTTGCGAGGCAA  
1750 1770 1790  
GTGCTCTACCACTGAGCTAAATCTCCAACCCCTGAAGGCCTCTTTCTTTCTGCCTCTGAT  
1810 1830 1850  
AGTCTATGACATTCTTTTTTCTACAATTTCGTATCAGGTGCACGAGCCTTATCCCATTGT  
1870 1890 1910  
AGGTTTCTAGGCAAGTTGACCGTTAGCTATTTTCCCTCTGAAGATTGATTTCGAGTTGC  
1930 1950 1970  
AGACTTGGCTAGACAAGCAGGGGTAGGTTATGGTAGTTTATTTAACAGACTGCCACCAGG  
1990 2010 2030  
AGTCCAGTGTTTCTTGTTCCCTCTGTAGTTGTACCTAAGCTGACTCCAAGTACATTAGTA  
2050 2070 2090  
TGAAAAATAATCAACAAATTTTATTTCCTTCTATCAACATTGGCTAGCTTTGTTTCAGGGC  
2110 2130 2150  
ACTAAAAGAACTACTATATGGAGAAAGAATTGATATTGCCCCCAACGTTCAACAACCCA  
2170 2190 2210  
ATAGTTTATCCAGCTGTCATGCCTGGTTCAGTGTCTACTGACTATGCGCCCTCTTATTAC  
2230 2250 2270  
TGCATGCAGTAATTCAACTGGAAATAGTAATAATAATAATAGAAATAAAATCTAGACTCC  
2290 2310 2330  
ATTGGATCTCTCTGAATATGGGAATATCTAACTTAAGAAGCTTTGAGATTTTCAGTTGTGT  
2350 2370 2390  
TAAAGGCTTTTATTAAAAAGCTGATGCTCTTCTGTAAAAGTTACTAATATATCTGTAAGA  
2410 2430  
CTATTACAGTATTGCTATTTATATCCATCCAG

FIG. 2D

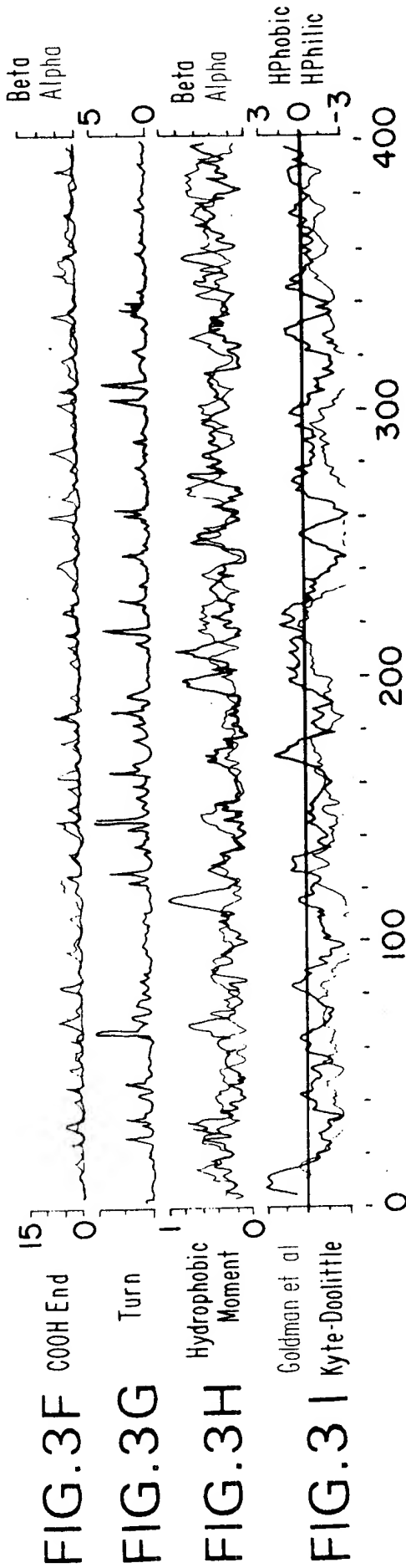
[illegible]

WZG

[illegible][illegible][illegible]







TITLE: COMBINATION THERAPY FOR CONDITIONS  
LEADING TO BONE LOSS  
INVENTORS: Boyle, et al.  
APPLN. NO: A-378CIP5

FIG.4A

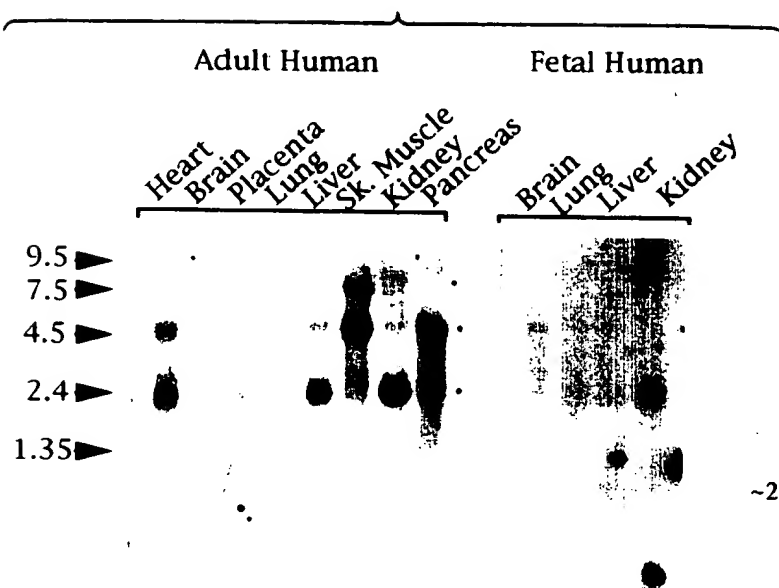
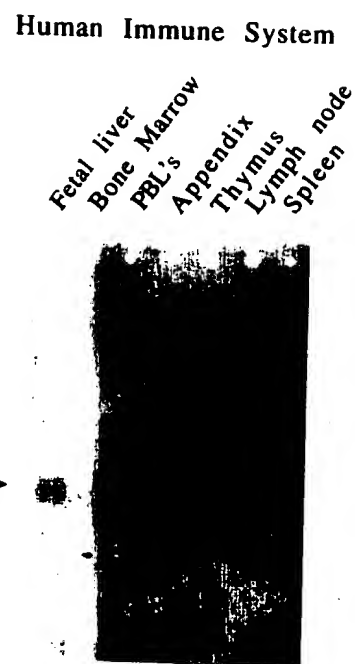
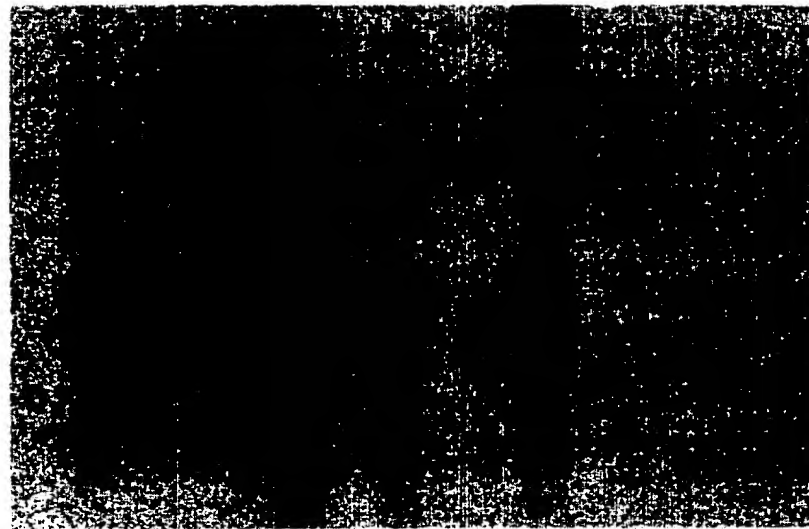


FIG.4B



TITLE: COMBINATION THERAPY FOR CONDITIONS  
LEADING TO BONE LOSS  
INVENTORS: Boyle, et al.  
APPLN. NO: A-378CIP5

FIG.5



2 11 16 17 22 28 33 38 45 Kb 1 12 18 30  
Transgenic Founders Controls

FIG.6A

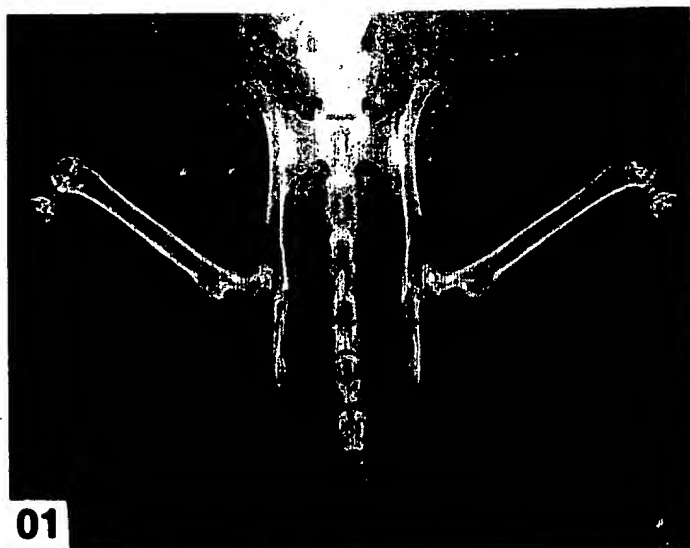


FIG.6B

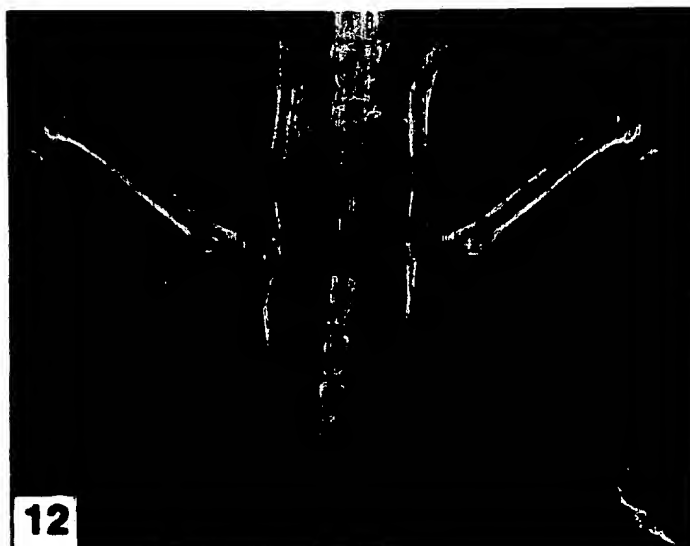
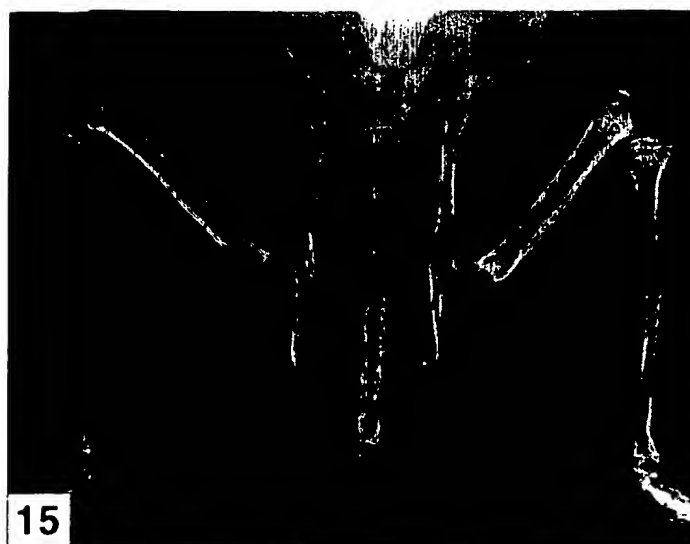


FIG.6C



TITLE: COMBINATION THERAPY FOR CONDITIONS  
LEADING TO BONE LOSS  
INVENTORS: Boyle, et al.  
APPLN. NO: A-378CIP5

FIG.6D

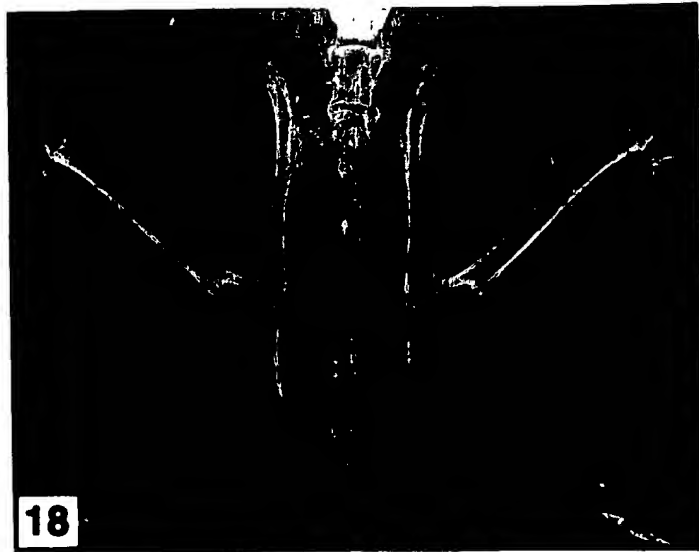


FIG.6E

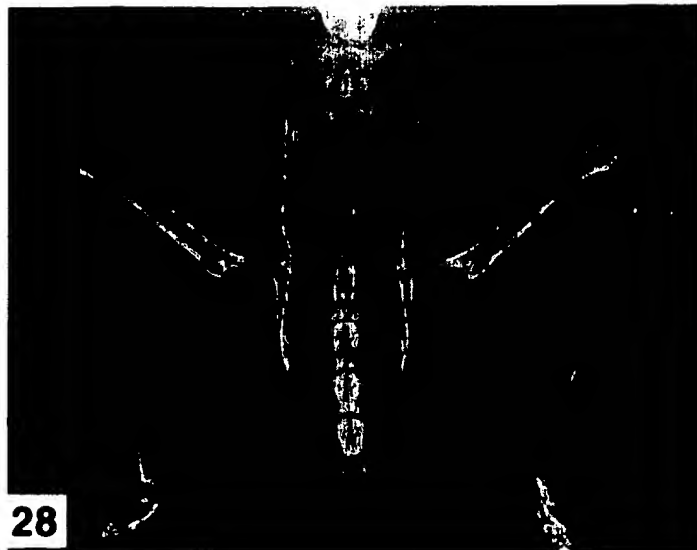


FIG.6F



TITLE: COMBINATION THERAPY FOR CONDITIONS  
LEADING TO BONE LOSS  
INVENTORS: Boyle, et al.  
APPLN. NO: A-378CIP5

FIG.6G

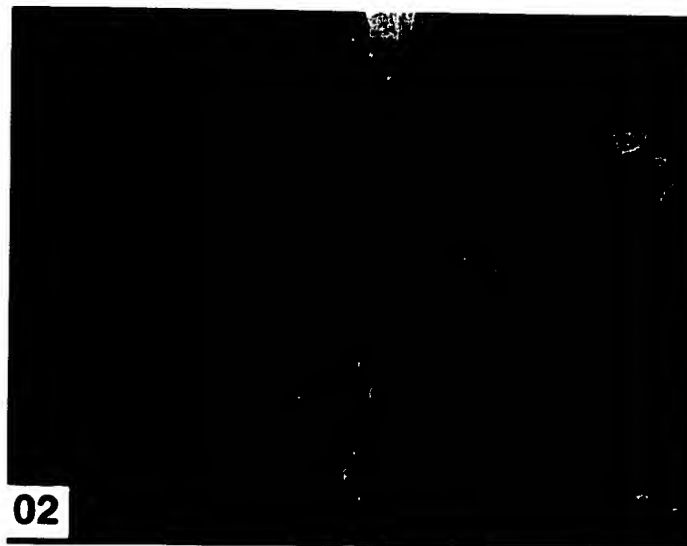
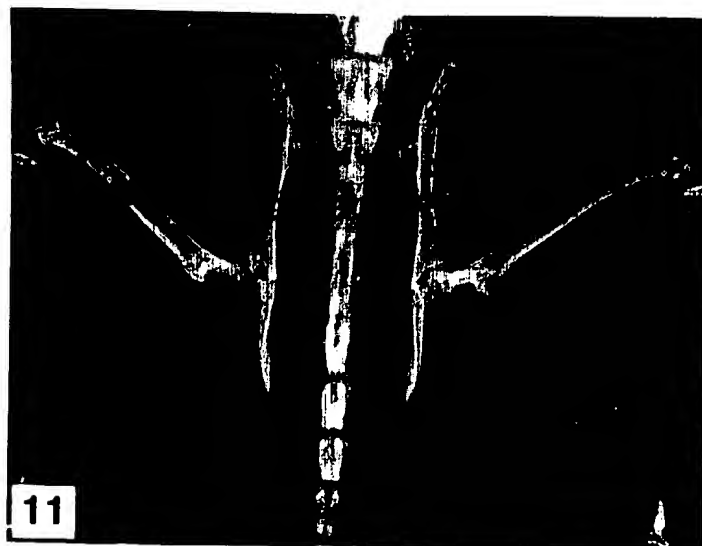


FIG.6H



TITLE: COMBINATION THERAPY FOR CONDITIONS  
LEADING TO BONE LOSS  
INVENTORS: Boyle, et al.  
APPLN. NO: A-378CIP5

FIG.6I

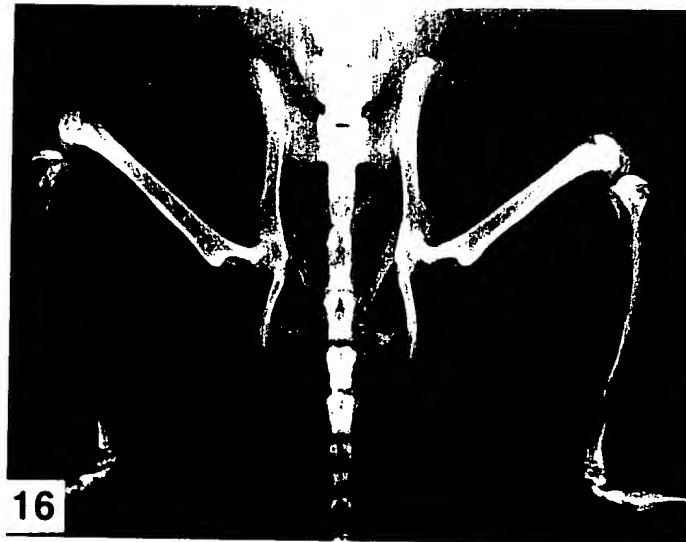
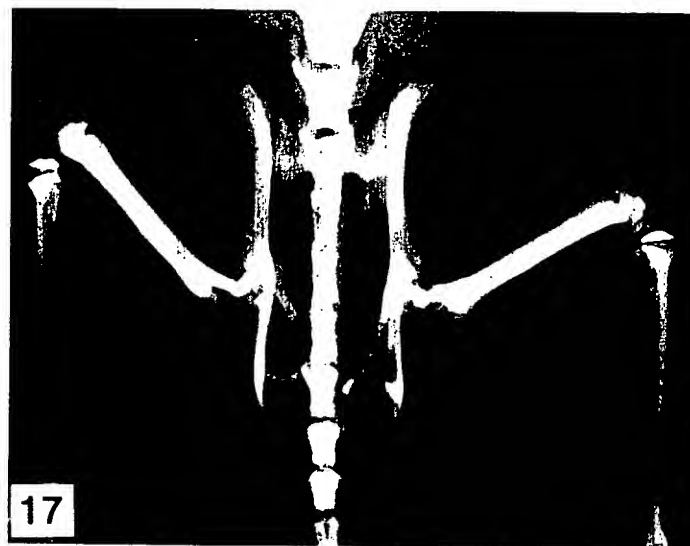


FIG.6J



TITLE: COMBINATION THERAPY FOR CONDITIONS  
LEADING TO BONE LOSS  
INVENTORS: Boyle, et al.  
APPLN. NO: A-378CIP5

FIG.7A

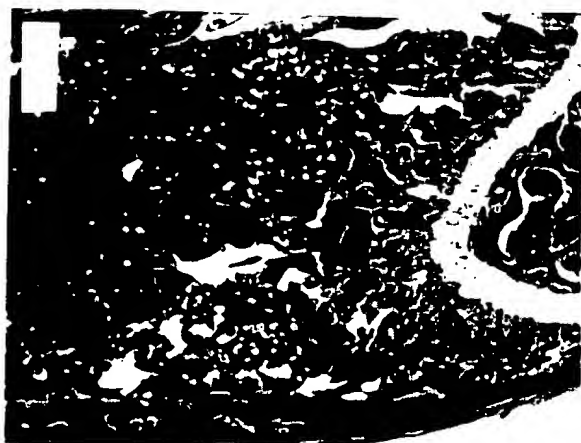


FIG.7B



FIG.7C



FIG.7D





TITLE: COMBINATION THERAPY FOR CONDITIONS  
LEADING TO BONE LOSS  
INVENTORS: Boyle, et al.  
APPLN. NO: A-378CIP5

FIG.7E



FIG.7F

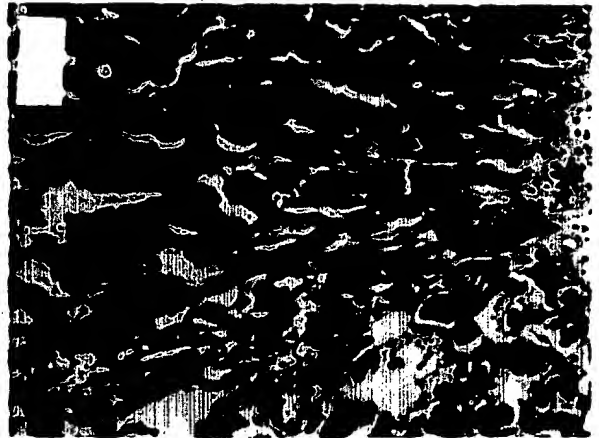
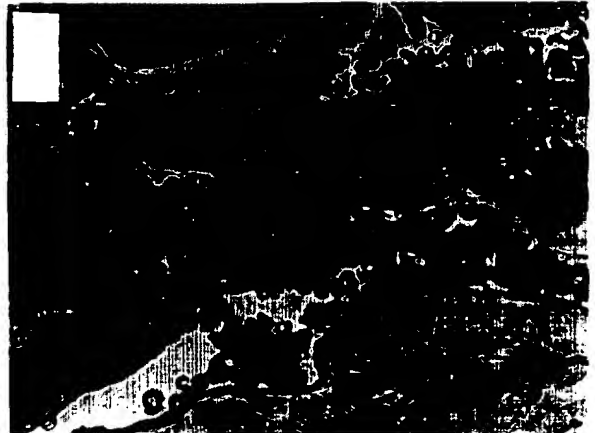


FIG.7G



FIG.7H



TITLE: COMBINATION THERAPY FOR CONDITIONS  
LEADING TO BONE LOSS  
INVENTORS: Boyle, et al.  
APPLN. NO: A-378CIP5

FIG.8A

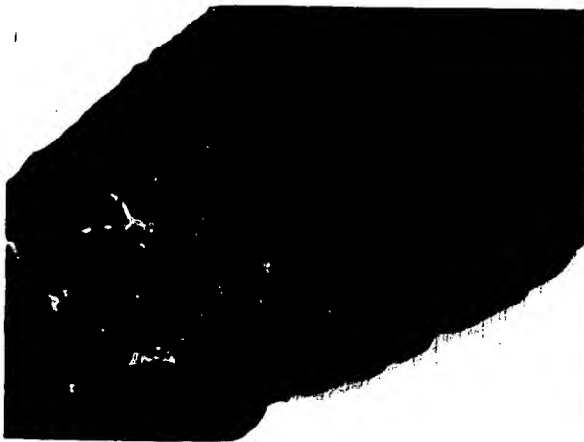


FIG.8B



FIG.8C

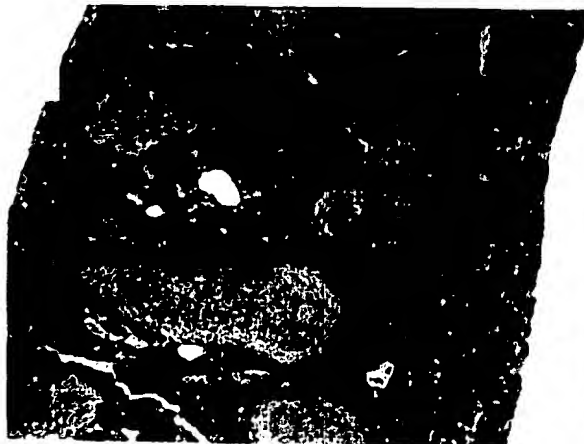
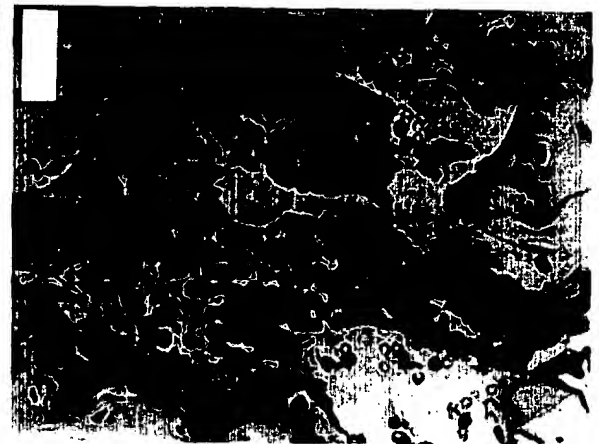


FIG.8D



TITLE: COMBINATION THERAPY FOR CONDITIONS  
LEADING TO BONE LOSS  
INVENTORS: Boyle, et al.  
APPLN. NO: A-378CIP5

## FIG.9A

```

      10              30              50
CCTTATATAARACGTCATGATTGCCTGGGCTGCAGAGACGCACCTAGCACTGACCCAGCG
      70              90              110
GCTGCCTCCTGAGGTTTCCCGAGGACCACAATGAACAAGTGGCTGTGCTGCGCACTCCTG
      130              150              170
      M N K W L C C A L L
GTGCTCCTGGACATCATTTGAATGGACAACCCAGGAAACCCTTCCTCCAAAGTACTTGCAT
      190              210              230
V L L D I I E W T T O E T L P P K Y L H
TATGACCCAGAACTGGTCATCAGCTCCTGTGTGACAAATGTGCTCCTGGCACCTACCTA
      250              270              290
Y D P E T G H Q L L C D K C A P G T Y L
AAACAGCACTGCACAGTGAGGAGGAAGACATTGTGTGTCCCTTGCCCTGACCACTCTTAT
      310              330              350
K Q H C T V R R K T L C V P C P D H S Y
ACGGACAGCTGGCACACCAGTGATGAGTGTGTGTATTGCAGCCCAGTGTGCAAGGAACTG
      370              390              410
T D S W H T S D E C V Y C S P V C K E L
CAGTCCGTGAAGCAGGAGTGCAACCGCACCCACAACCGAGTGTGTGAGTGTGAGGAAGGG
      430              450              470
Q S V K Q E C N R T H N R V C E C E E G
CGTTACCTGGAGATCGAATTCTGCTTGAAGCACCGGAGCTGTCCCCCGGGCTCCGGCGTG
      490              510              530
R Y L E I E F C L K H R S C P P G S G V
GTGCAAGCTGGAACCCCAGAGCGAAACACAGTTTGCAAAAAATGTCCAGATGGGTTCTTC
      550              570              590
V Q A G T P E R N T V C K K C P D G F F
TCAGGTGAGACTTCATCGAAAGCACCCCTGTATAAAACACACGAACTGCAGCACATTTGGC
      610              630              650
S G E T S S K A P C I K H T N C S T F G
CTCCTGCTAATTCAGAAAGGAAATGCAACACATGACAACGTGTGTTCCGGAAACAGAGAA
      670              690              710
L L L I Q K G N A T H D N V C S G N R E
GCCACGCAAAAAGTGTGGAATAGATGTCAACCCTGTGTGAAGAGGCCTTCTTCAGGTTTGCT
      730              750              770
A T Q K C G I D V T L C E E A F F R F A
GTTCTACCAAGATTATACCAAATTGGCTGAGTGTTTTGGTGGACAGTTTGCCTGGGACC
V P T K I I P N W L S V L V D S L P G T

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TITLE: COMBINATION THERAPY FOR CONDITIONS  
LEADING TO BONE LOSS  
INVENTORS: Boyle, et al.  
APPLN. NO: A-378CIP5

## FIG.9B

```

      790              810              830
AAAGTGAATGCCGAGAGTGTAGAGAGGATAAAACGGAGACACAGCTCACAAAGAGCAAACC
K  V  N  A  E  S  V  E  R  I  K  R  R  H  S  S  Q  E  Q  T
      850              870              890
TTCCAGCTGCTGAAGCTGTGGAAACATCAAACAGAGACCAGGAAATGGTGAAGAAGATC
F  Q  L  L  K  L  W  K  H  Q  N  R  D  Q  E  M  V  K  K  I
      910              930              950
ATCCAAGACATTGACCTCTGTGAAAGCAGCGTGCAGCGGCATCTCGGCCACTCGAACCTC
I  Q  D  I  D  L  C  E  S  S  V  Q  R  H  L  G  H  S  N  L
      970              990              1010
ACCACAGAGCAGCTTCTTGCCTTGATGGAGAGCCTGCCTGGGAAGAAGATCAGCCCAGAA
T  T  E  Q  L  L  A  L  M  E  S  L  P  G  K  K  I  S  P  E
      1030             1050             1070
GAGATTGAGAGAACGAGAAAGACCTGCAAATCGAGCGAGCAGCTCCTGAAGCTACTCAGT
E  I  E  R  T  R  K  T  C  K  S  S  E  Q  L  L  K  L  L  S
      1090             1110             1130
TTATGGAGGATCAAAAATGGTGACCAAGACACCTTGAAGGGCCTGATGTATGCCCTCAAG
L  W  R  I  K  N  G  D  Q  D  T  L  K  G  L  M  Y  A  L  K
      1150             1170             1190
CACTTGAAAAACATCCCACCTTTCCCAAAACTGTCACCCACAGTCTGAGGAAGACCATGAGG
H  L  K  T  S  H  F  P  K  T  V  T  H  S  L  R  K  T  M  R
      1210             1230             1250
TTCCTGCACAGCTTCACAATGTACAGACTGTATCAGAAGCTCTTTTATAGAAATGATAGGG
F  L  H  S  F  T  M  Y  R  L  Y  Q  K  L  F  L  E  M  I  G
      1270             1290             1310
AATCAGGTTCAATCCGTGAAAATAAGCTGCTTATAACTAGGAATGGTCACTGGGCTGTTT
N  Q  V  Q  S  V  K  I  S  C  L

```

CTTCA

TITLE: COMBINATION THERAPY FOR CONDITIONS  
LEADING TO BONE LOSS  
INVENTORS: Boyle, et al.  
APPLN. NO: A-378CIP5

## FIG.9C

```

      10              30              50
GTATATATAACGTGATGAGCGTACGGGTGCGGAGACGCACCGGAGCGCTCGCCCAGCCGC
      70              90              110
CGYCTCCAAGCCCCTGAGGTTTCCGGGGACCACAATGAACAAGTTGCTGTGCTGCGCGCT
                                M N K L L C C A L
      130              150              170
CGTGT'TTCTGGACATCTCCAT'TAAGTGGACCACCCAGGAAACGTT'TCCTCCAAAGTACCT
V F L D I S I K W T T Q E T F P P K Y L
      190              210              230
TCATTATGACGAAGAAACCTCTCATCAGCTGTTGTGTGACAAATGTCCTCCTGGTACCTA
H Y D E E T S H Q L L C D K C P P G T Y
      250              270              290
CCTAAAACAACACTGTACAGCAAAGTGGAAGACCGTGTGCGCCCCCTTGCCCTGACCACTA
L K Q H C T A K W K T V C A P C P D H Y
      310              330              350
CTACACAGACAGCTGGCACACCAGTGACGAGTGTCTATACTGCAGCCCCGTGTGCAAGGA
Y T D S W H T S D E C L Y C S P V C K E
      370              390              410
GCTGCAGTACGTCAAGCAGGAGTGCAATCGCACCCACAACCGCGTGTGCGAATGCAAGGA
L Q Y V K Q E C N R T H N R V C E C K E
      430              450              470
AGGGCGCTACCTTGAGATAGAGTTCTGCTTGAAACATAGGAGCTGCCCTCCTGGATTTGG
G R Y L E I E F C L K H R S C P P G F G
      490              510              530
AGTGGTGCAAGCTGGAACCCCAAGCGGAAATACAGTTTGCAAAAGATGTCCAGATGGGTT
V V Q A G T P E R N T V C K R C P D G F
      550              570              590
CTTCTCAAATGAGACGTCATCTAAAGCACCCCTGTAGAAAACACACAAATTGCAGTGTCTT
F S N E T S S K A P C R K H T N C S V F
      610              630              650
TGGTCTCCTGCTAACTCAGAAAGGAAATGCAACACACGACAACATATGTTCCGGAAACAG
G L L L T Q K G N A T H D N I C S G N S
      670              690              710
TGAATCAACTCAAAAATGTGGAATAGATGTTACCCTGTGTGAGGAGGCATTCTTCAGGTT
E S T Q K C G I D V T L C E E A F F R F
      730              750              770
TGCTGTTCTACAAAGTTTACGCCTAACTGGCTTAGTGTCTTGGTAGACAATTTGCCTGG
A V P T K F T P N W L S V L V D N L P G

```

TITLE: COMBINATION THERAPY FOR CONDITIONS  
LEADING TO BONE LOSS  
INVENTORS: Boyle, et al.  
APPLN. NO: A-378CIP5

## FIG.9D

```

      790              810              830
CACCAAAGTAAACGCAGAGAGTGTAGAGAGGATAAAACGGCAACACAGCTCACAAGAACA
T K V N A E S V E R I K R Q H S S Q E Q
      850              870              890
GACTTTCAGCTGCTGAAGTTATGGAAACATCAAAACAAAGACCAAGATATAGTCAAGAA
T F Q L L K L W K H Q N K D Q D I V K K
      910              930              950
GATCATCCAAGATATTGACCTCTGTGAAAACAGCGTGCAGCGGCACATTGGACATGCTAA
I I Q D I D L C E N S V Q R H I G H A N
      970              990              1010
CCTCACCTTCGAGCAGCTTCGTAGCTTGATGGAAAGCTTACCGGGAAAGAAAGTGGGAGC
L T F E Q L R S L M E S L P G K K V G A
      1030              1050              1070
AGAAGACATTGAAAAACAATAAAGGCATGCAAACCCAGTGACCAGATCCTGAAGCTGCT
E D I E K T I K A C K P S D Q I L K L L
      1090              1110              1130
CAGTTTGTGGCGAATAAAAAATGGCGACCAAGACACCTTGAAGGGCCTAATGCACGCACT
S L W R I K N G D Q D T L K G L M H A L
      1150              1170              1190
AAAGCACTCAAAGACGTACCACTTTCCCAAAACTGTCACTCAGAGTCTAAAGAAGACCAT
K H S K T Y H F P K T V T Q S L K K T I
      1210              1230              1250
CAGGTTCTTCACAGCTTCACAATGTACAAATTGTATCAGAAGTTATTTTAGAAATGAT
R F L H S F T M Y K L Y Q K L F L E M I
      1270              1290              1310
AGGTAACCAGGTCCAATCAGTAAAAATAAGCTGCTTATAACTGGAAATGGCCATTGAGCT
G N Q V Q S V K I S C L
      1330              1350
GTTTCCTCACAATTGGCGAGATCCCATGGATGATAA
```

FIG. 9E

osteo.frg	M N K W L C C A L L V L L D I I E W T T Q E T L P P K Y L H Y D P E T G H Q L L C D K K C A P G T Y L	50
osteo.frg	M N K W L C C A L L V L L D I I E W T T Q E T L P P K Y L H Y D P E T G R Q L L C D K K C A P G T Y L	50
osteo.frg	M N K W L C C A L L V L L D I I E W T T Q E T L P P K Y L H Y D E T S H Q L L C D K K C P P G T Y L	50
osteo.frg	K Q H C T V R R K T L C V P C P D H S Y T D S W H T S D E C V Y C S P V C K E L Q S V K Q E C N R T	100
osteo.frg	K Q H C T V R R K T L C V P C P D Y S Y T D S W H T S D E C V Y C S P V C K E L Q T V K Q E C N R T	100
osteo.frg	K Q H C T A K W K T V C A P C P D H Y Y T D S W H T S D E C L Y C S P V C K E L Q Y V K Q E C N R T	100
osteo.frg	H N R V C E C E E G R Y L E I E F C L K H R S C P P G S G V V Q A G T P E R N T V C K K C P D G F F	150
osteo.frg	H N R V C E C E E G R Y L E L E F C L K H R S C P P G L G V L Q A G T P E R N T V C K R C P D G F F	150
osteo.frg	H N R V C E C K E G R Y L E I E F C L K H R S C P P G F G V V Q A G T P E R N T V C K R C P D G F F	150
osteo.frg	S G E T S S K A P C I K H T N C S T F G L L L I Q K G N A T H D N V C S G N R E A T Q K C G I D V T	200
osteo.frg	S G E T S S K A P C R K H T N C S S L G L L L I Q K G N A T H D N V C S G N R E A T Q N C G I D V T	200
osteo.frg	S N E T S S K A P C R K H T N C S V F G L L L T Q K G N A T H D N I C S G N S E S T Q K C G I D V T	200

FIG. 9F

osteo.frg	L C E E A F F R F A V P T K I I P N W L S V L V D S L P G T K V N A E S V E R I K R R R H S S Q E Q T	250
osteo.frg	L C E E A F F R F A V P T K I I P N W L S V L V D S L P G T K V N A E S V E R I K R R R H S S Q E Q T	250
osteo.frg	L C E E A F F R F A V P T K I I P N W L S V L V D S L P G T K V N A E S V E R I K R R R H S S Q E Q T	250
osteo.frg	F Q L L K L W K K H Q N R D Q E M V K K I I Q D I D L C E S S V Q R H L G H S N L T T E Q L L A L M E	300
osteo.frg	F Q L L K L W K K H Q N R D Q E M V K K I I Q D I D L C E S S V Q R H L G H S N L T T E Q L L A L M E	300
osteo.frg	F Q L L K L W K K H Q N R D Q E M V K K I I Q D I D L C E S S V Q R H L G H S N L T T E Q L L A L M E	300
osteo.frg	S L P G K K I S P E E I E R T R K T C K S S E Q L L K L L S L W R I K N G D Q D T L K G L M Y A L K	350
osteo.frg	S L P G K K I S P D E I E R T R K T C K P S E Q L L K L L S L W R I K N G D Q D T L K G L M Y A L K	350
osteo.frg	S L P G K K V G A E D I E K T I K A C K P S D Q I L K L L S L W R I K N G D Q D T L K G L M Y A L K	350
osteo.frg	H L K T S H F P K T V T H S L R K T M R F L H S F T M Y R L Y Q K L F L E M I G N Q V Q S V K I S C	400
osteo.frg	H L K A Y H F P K T V T H S L R K T I R F L H S F T M Y R L Y Q K L F L E M I G N Q V Q S V K I S C	400
osteo.frg	H S K T Y H F P K T V T Q S L K K T I R F L H S F T M Y R L Y Q K L F L E M I G N Q V Q S V K I S C	400
osteo.frg	L	401
osteo.frg	L	401
osteo.frg	L	401



TITLE: COMBINATION THERAPY FOR CONDITIONS  
LEADING TO BONE LOSS  
INVENTORS: Boyle, et al.  
APPLN. NO: A-378CIP5

FIG. 10

1tnrr	C	P	Q	-	G	K	Y	I	H	P	Q	N	N	S	I	C	C	T	K	C	H	K	C	G	T	Y	L	Y	N	D	C	P	G	P	G	Q	D	T	D	C	R	E	C	E	S	G	S	F	T	A	S	49
noste	P	P	K	Y	L	H	Y	D	E	E	T	S	H	Q	L	L	C	D	K	C	P	P	C	G	T	Y	L	K	Q	H	C	T	A	K	-	W	K	T	V	C	A	P	C	P	D	H	Y	Y	T	D	S	49
1tnrr	E	N	H	L	R	H	C	L	S	C	S	-	K	C	R	K	E	M	G	Q	V	E	I	S	S	C	T	V	D	R	D	T	V	C	G	C	R	K	N	Q	Y	R	H	Y	W	S	E	N	L	F	98	
noste	W	H	T	S	D	E	C	L	Y	C	S	P	V	C	-	K	E	L	Q	Y	V	K	-	Q	E	C	C	N	R	T	H	N	R	V	C	E	C	K	E	G	R	Y	L	E	I	-	-	E	-	F	93	
1tnrr	Q	C	F	N	C	S	L	C	L	N	G	-	T	V	H	L	S	C	Q	E	K	Q	N	T	V	C	T	-	C	H	A	G	F	F	L	R	E	-	-	-	N	E	C	V	S	C	139					
noste	-	C	L	K	H	R	S	C	P	P	G	F	G	V	V	Q	A	G	T	P	E	R	N	T	V	C	K	R	C	P	D	G	F	F	S	N	E	T	S	S	K	A	P	C	R	K	H	139				

TITLE: COMBINATION THERAPY FOR CONDITIONS  
LEADING TO BONE LOSS  
INVENTORS: Boyle, et al.  
APPLN. NO: A-378CIP5

FIG. II

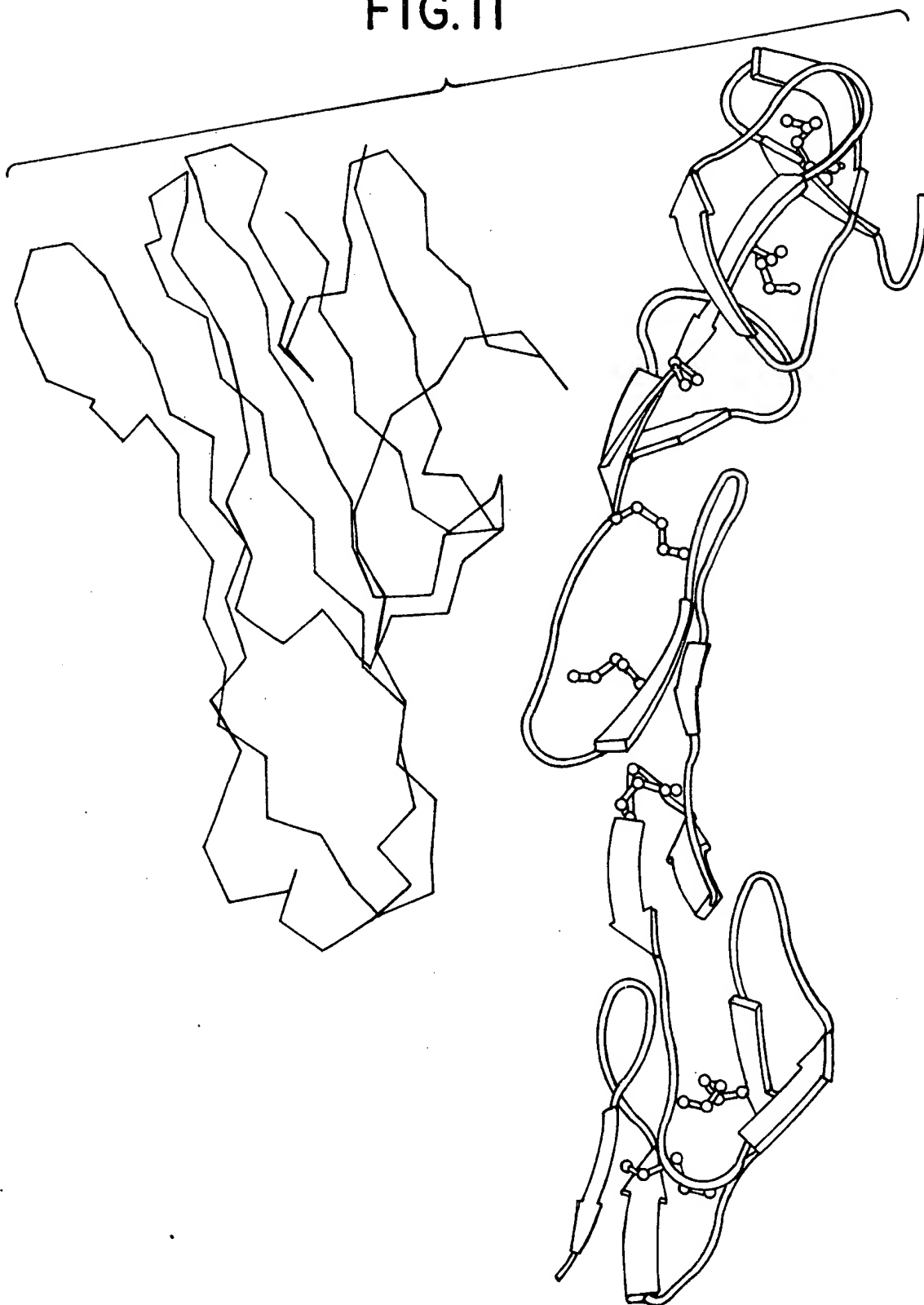


FIG. 12A

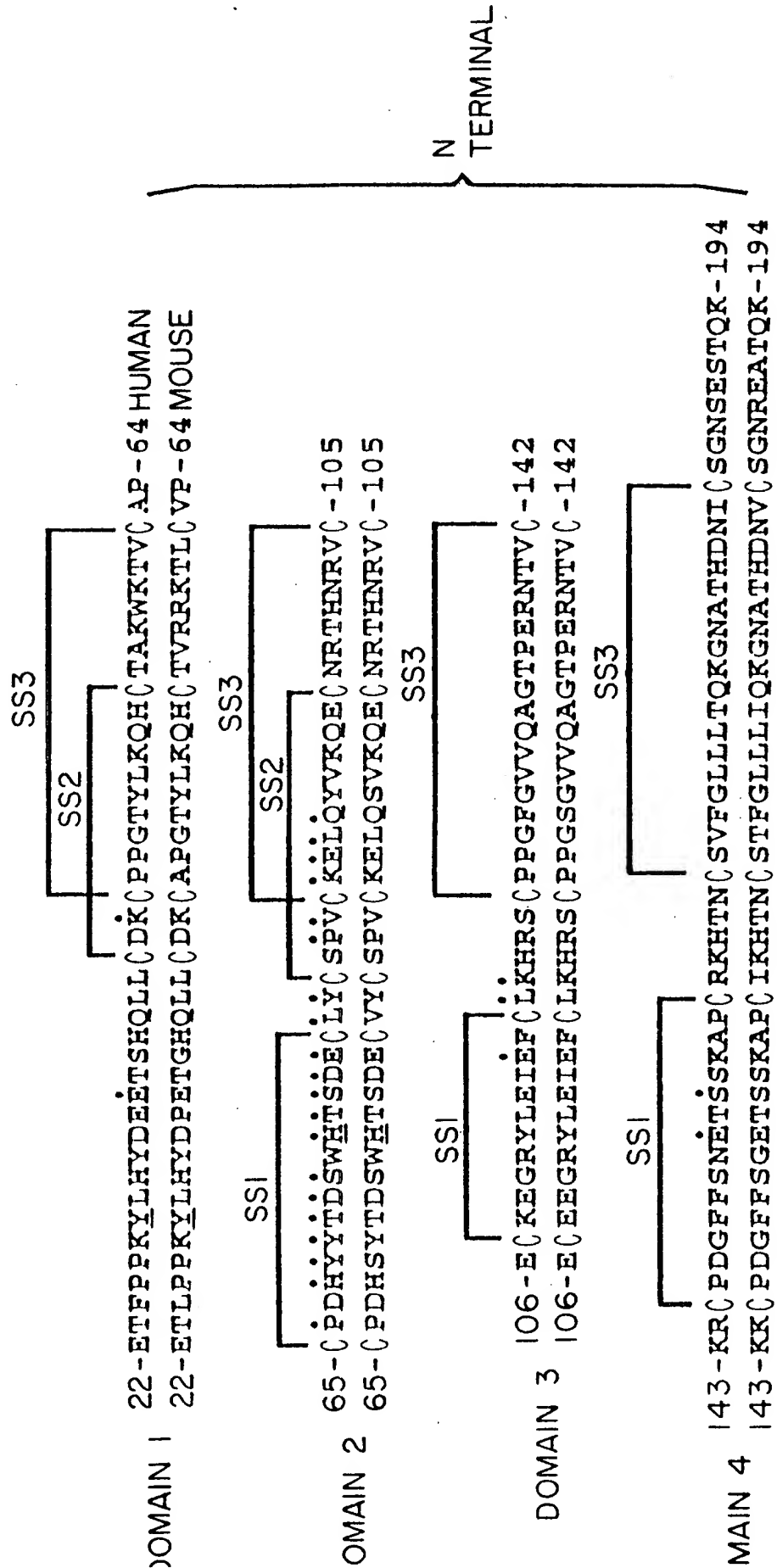


FIG. 12B

195-CGIDVTLC<sup>C</sup>EEAFFRFAVPTKFTPNWLSVLVDNLPGTKVNAESVERIKRQHSS-246  
195-CGIDVTLC<sup>C</sup>EEAFFRFAVPTKIIIPNWLSVLVDNLPGTKVNAESVERIKRRHSS-246  
247-QEQTFFQLLKLWKHQNKDQDI<sup>C</sup>VKKIIQDIDID<sup>C</sup>ENSVQRHIGHANLTPEQLRSL-298  
247-QEQTFFQLLKLWKHQNRDQEMVKKIIQDIDID<sup>C</sup>CESSVQRHLGHSNLTTEQLLAL-298  
299-MESLPGKKVGAEDIEKTIKAC<sup>C</sup>KPSDQILKLLSLWRIKNGDQDTLKGLMHALK-350  
299-MESLPGKKISPEEIERTRKT<sup>C</sup>KSSEQLLKL<sup>C</sup>SLWRIKNGDQDTLKGLMYALK-350  
351-HSKTYHFPKTVTQSLKKTIRFLHSFTMYKLYQKLFLEMIGNQVQSVKIS<sup>C</sup>L-401  
351-HLKTSHPKTVTHSLRK<sup>C</sup>TMRF<sup>C</sup>LHSFTMYRLYQKLFLEMIGNQVQSVKIS<sup>C</sup>L-401

C  
TERMINAL

FIG. 13A



FIG. 13B

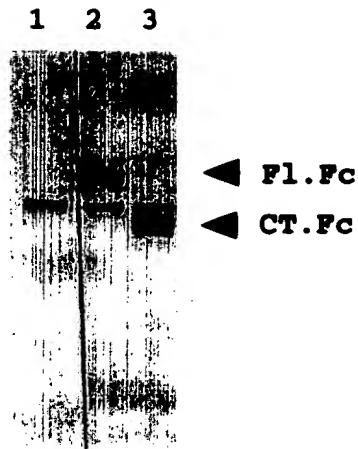


FIG. 13C

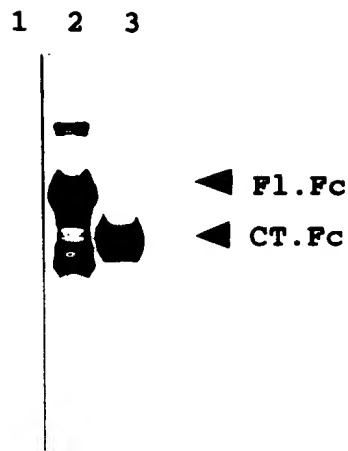


FIG.14A

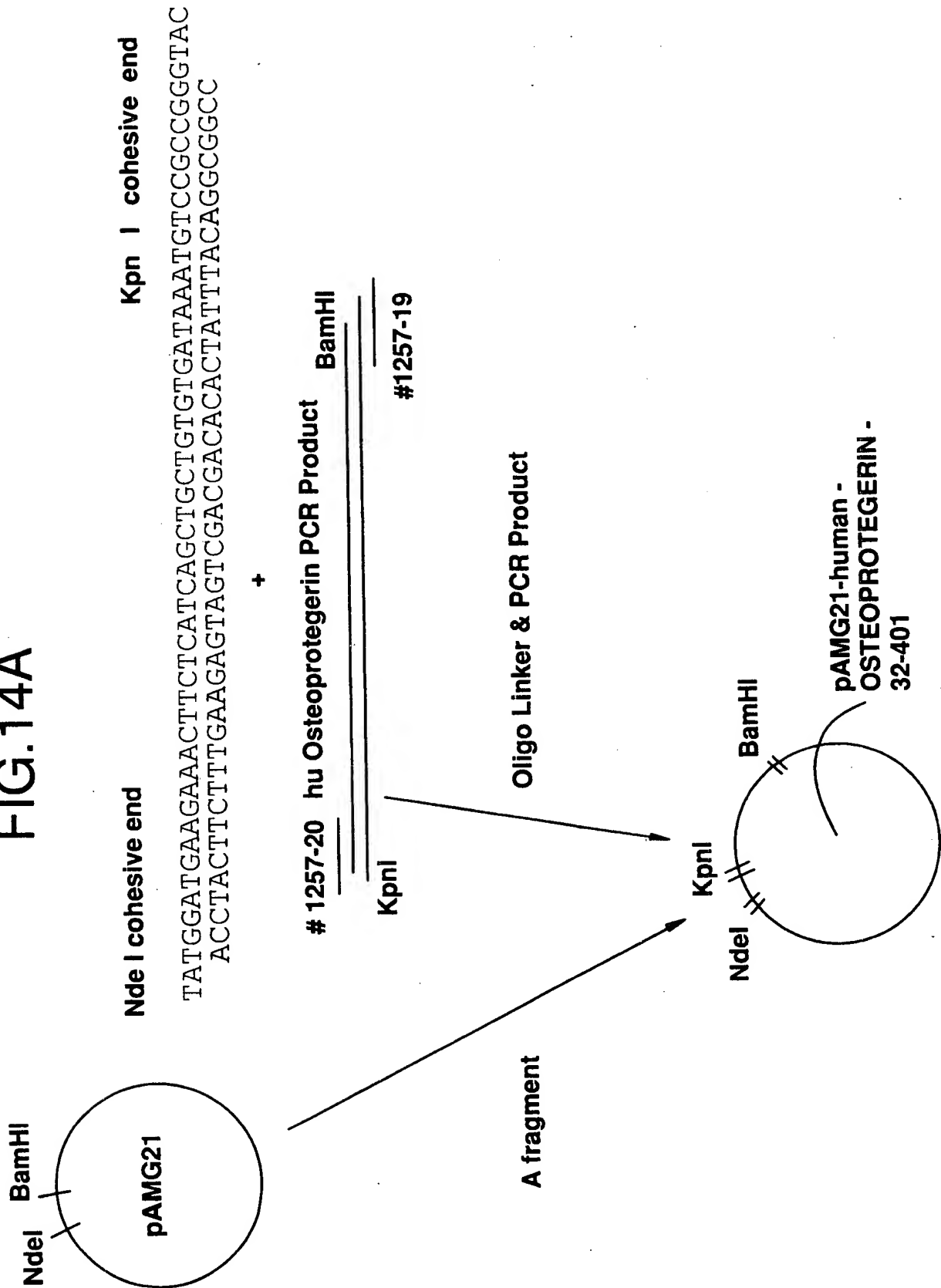
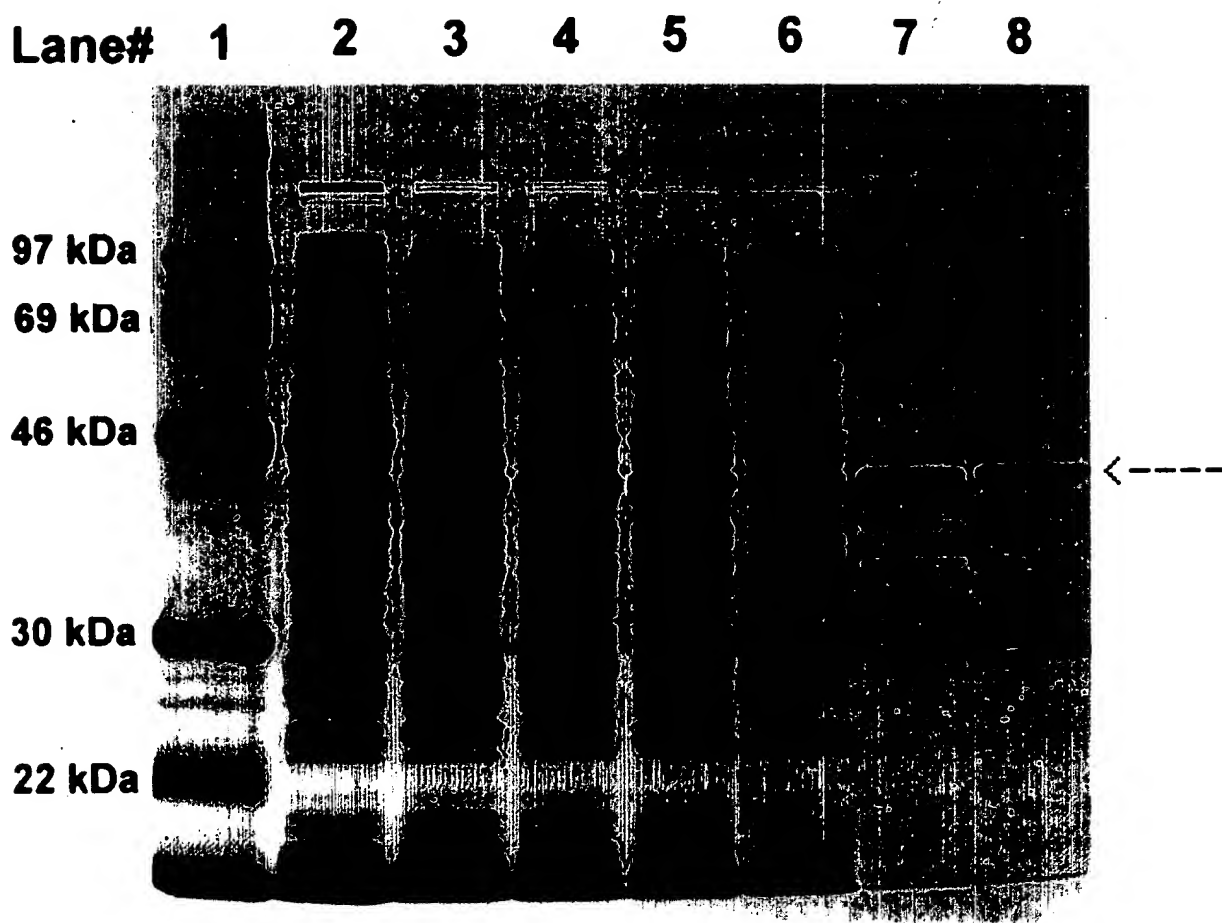
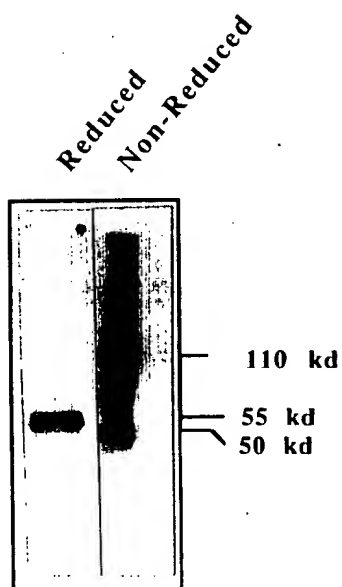


FIG. 14B



TITLE: COMBINATION THERAPY FOR CONDITIONS  
LEADING TO BONE LOSS  
INVENTORS: Boyle, et al.  
APPLN. NO: A-378CIP5

FIG.15





TITLE: COMBINATION THERAPY FOR CONDITIONS  
LEADING TO BONE LOSS  
INVENTORS: Boyle, et al.  
APPLN. NO: A-378CIP5

FIG.16A

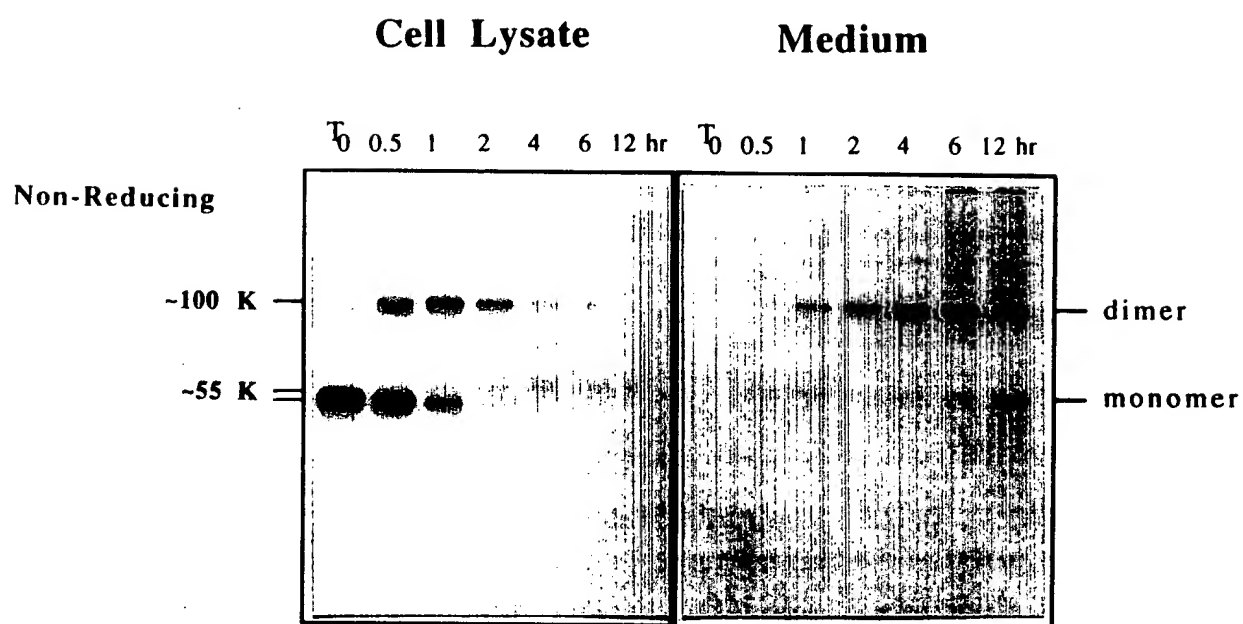
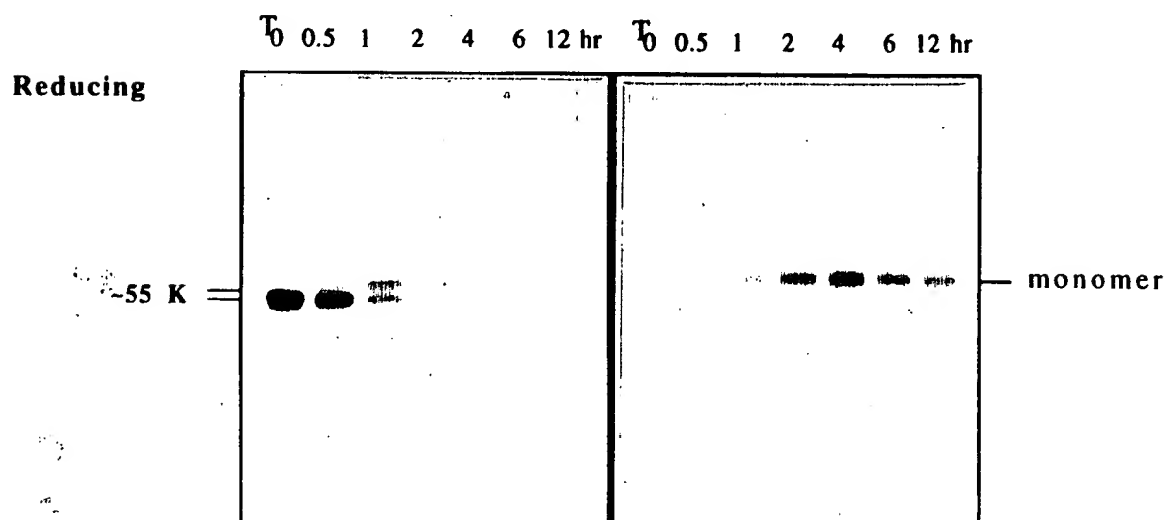
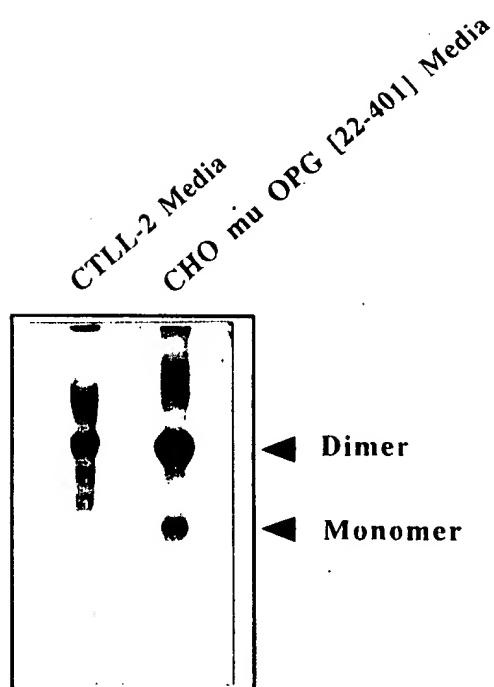


FIG.16B



TITLE: COMBINATION THERAPY FOR CONDITIONS  
LEADING TO BONE LOSS  
INVENTORS: Boyle, et al.  
APPLN. NO: A-378CIP5

FIG.17



INVENTORS: Boyle, et al.  
APPLN. NO: A-378CIP5

FIG. 18

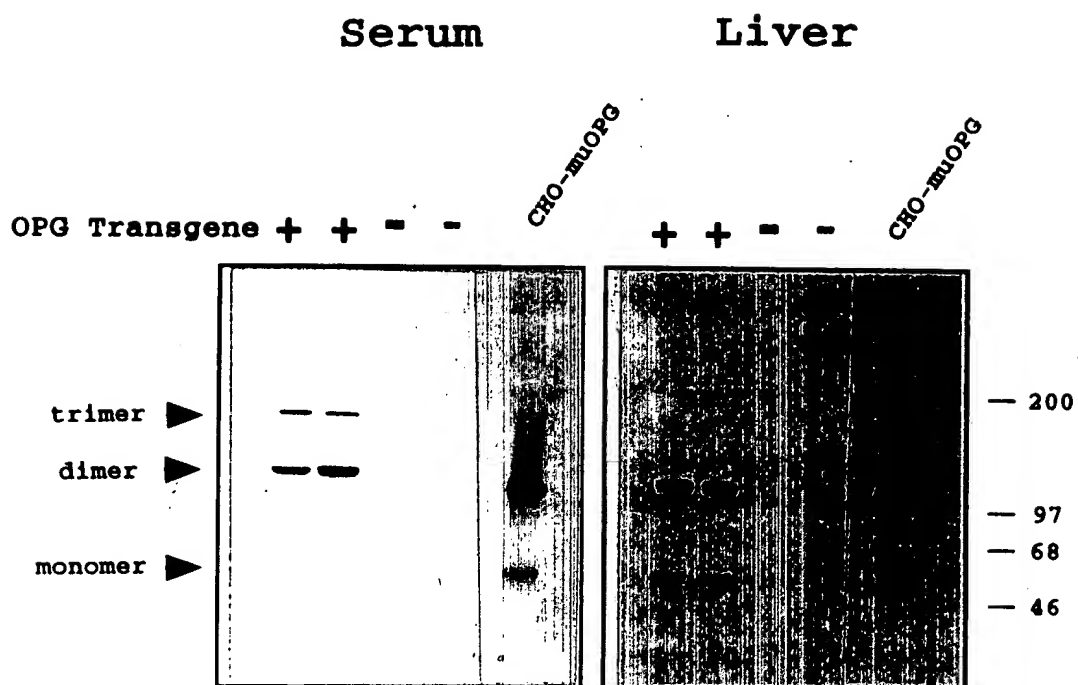


FIG.19A

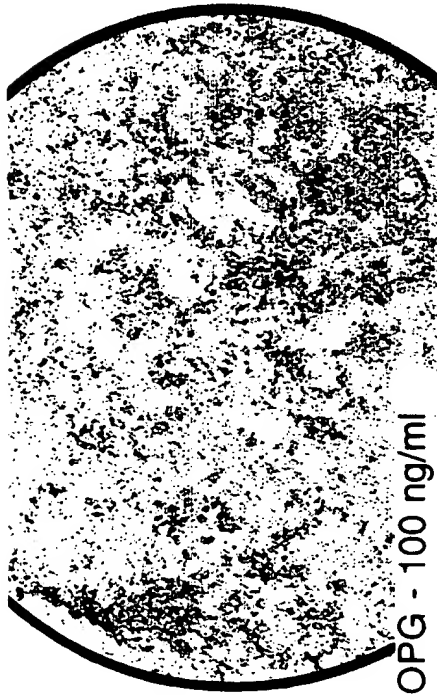


FIG.19B

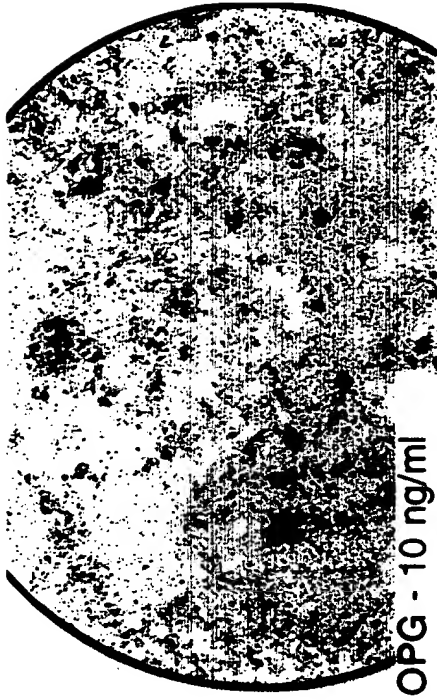


FIG.19C

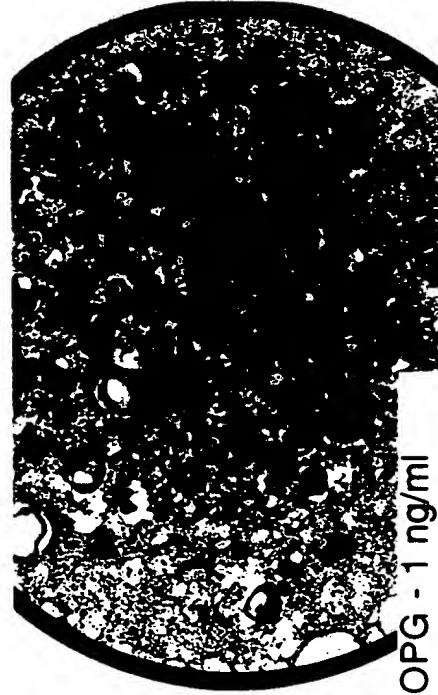


FIG.19D

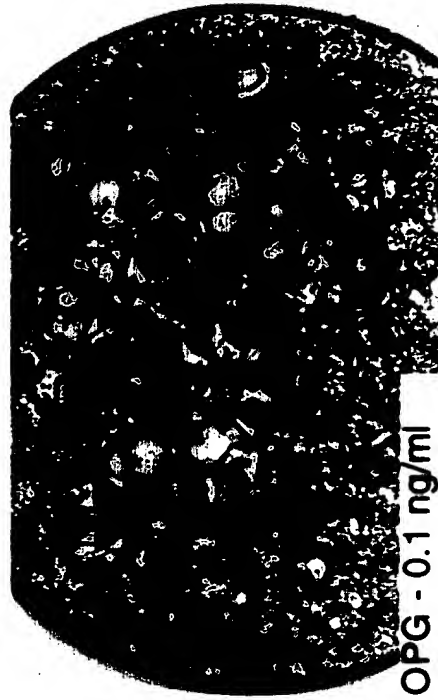


FIG. 19F

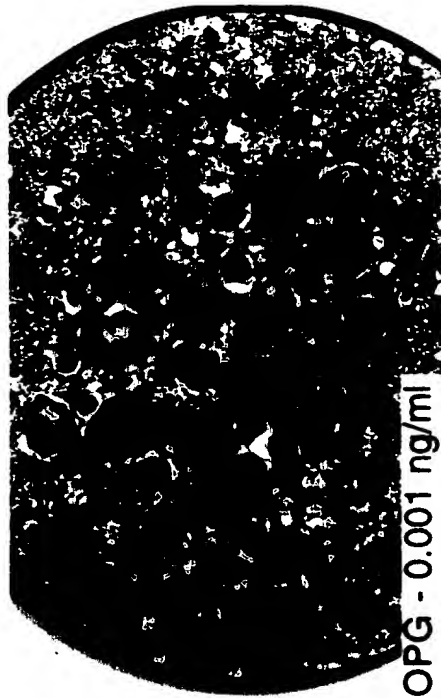


FIG. 19E

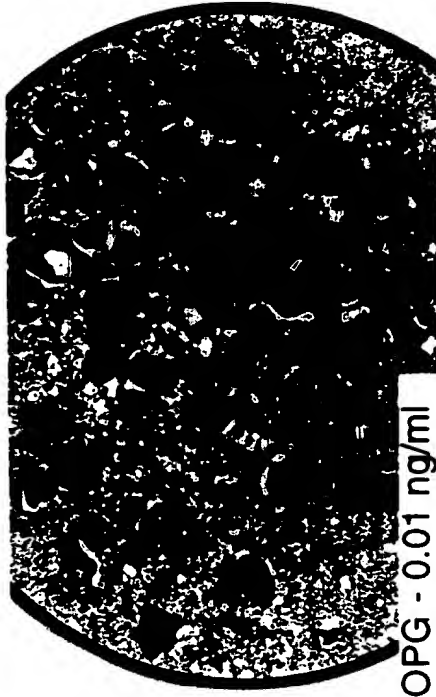


FIG. 19G



TITLE: COMBINATION THERAPY FOR CONDITIONS  
LEADING TO BONE LOSS  
INVENTORS: Boyle, et al.  
APPLN. NO: A-378CIP5

FIG.20

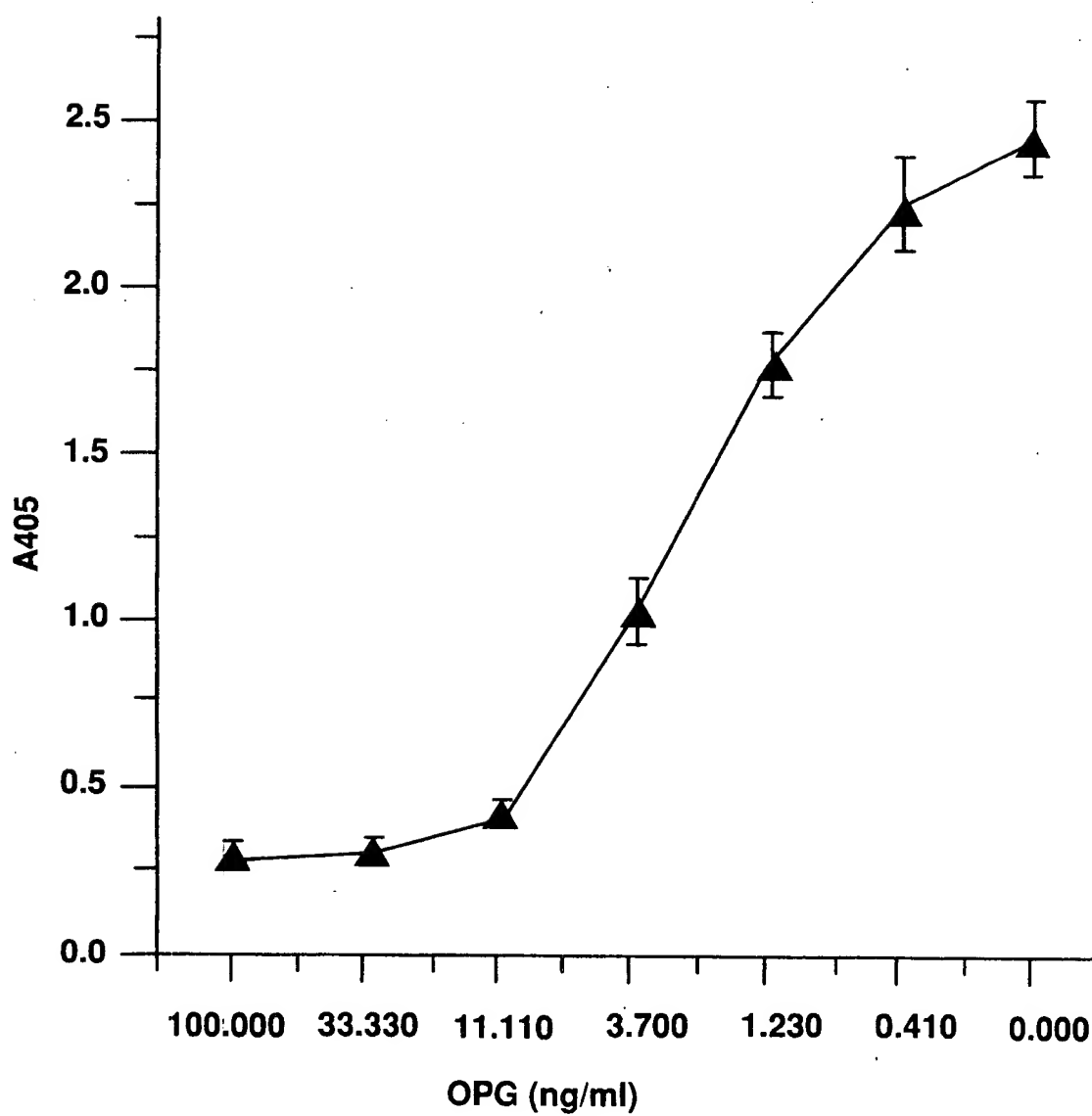
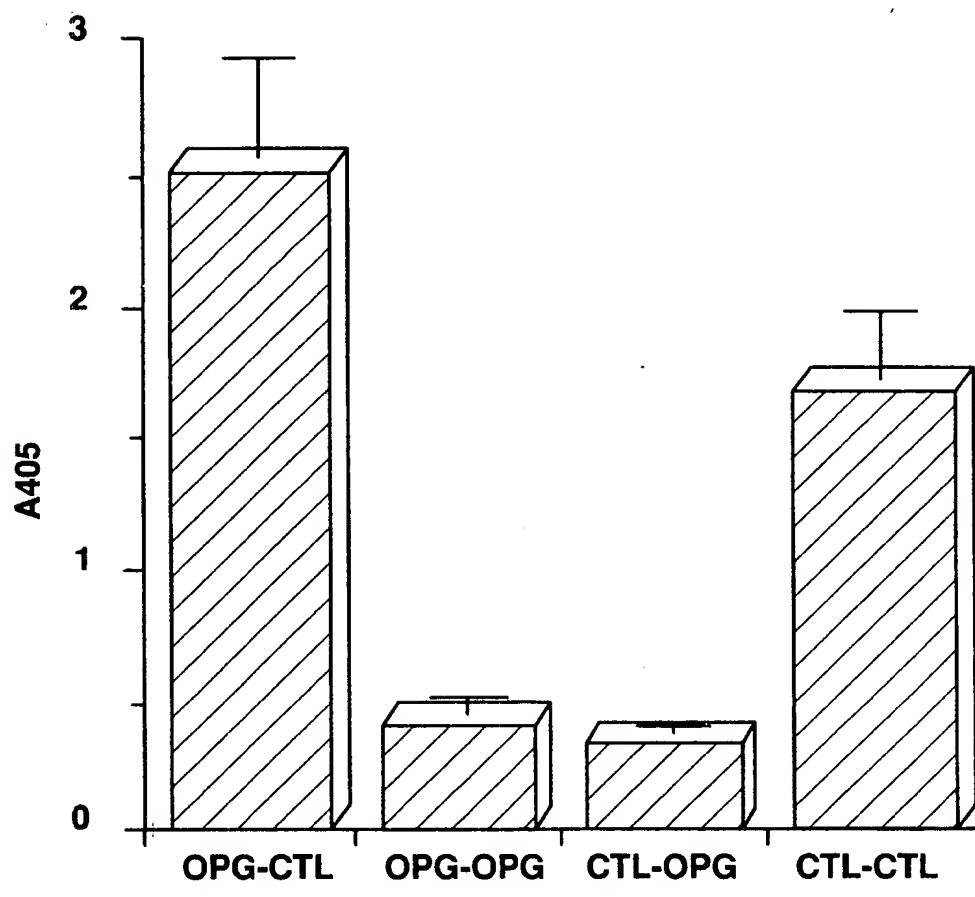


FIG.21



Legend

**Growth**  
Bone marrow  
cells  
CSF -1

4 days

**Intermediate**  
PGE2 + CSF-1

2 days

**Terminal**  
ST2 cells  
1,25 (OH)2 D3  
Dexamethasone

8 - 10 days

Groups

CTL - CTL

OPG - CTL

OPG - OPG

OPG - OPG

OPG

100 ng/ml

100 ng/ml

OPG

100 ng/ml

100 ng/ml

FIG.22A

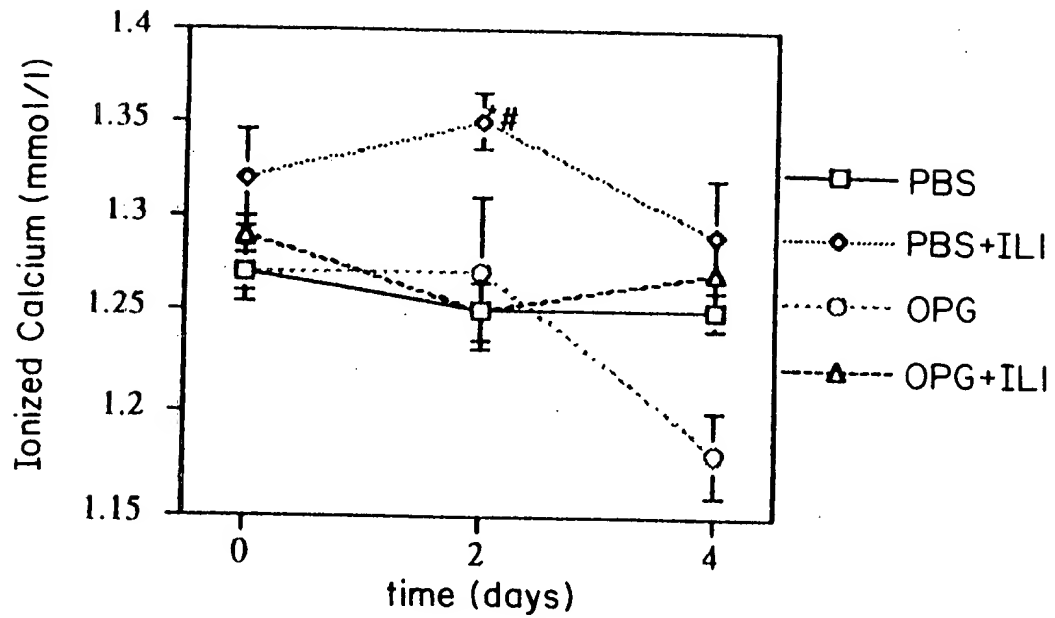
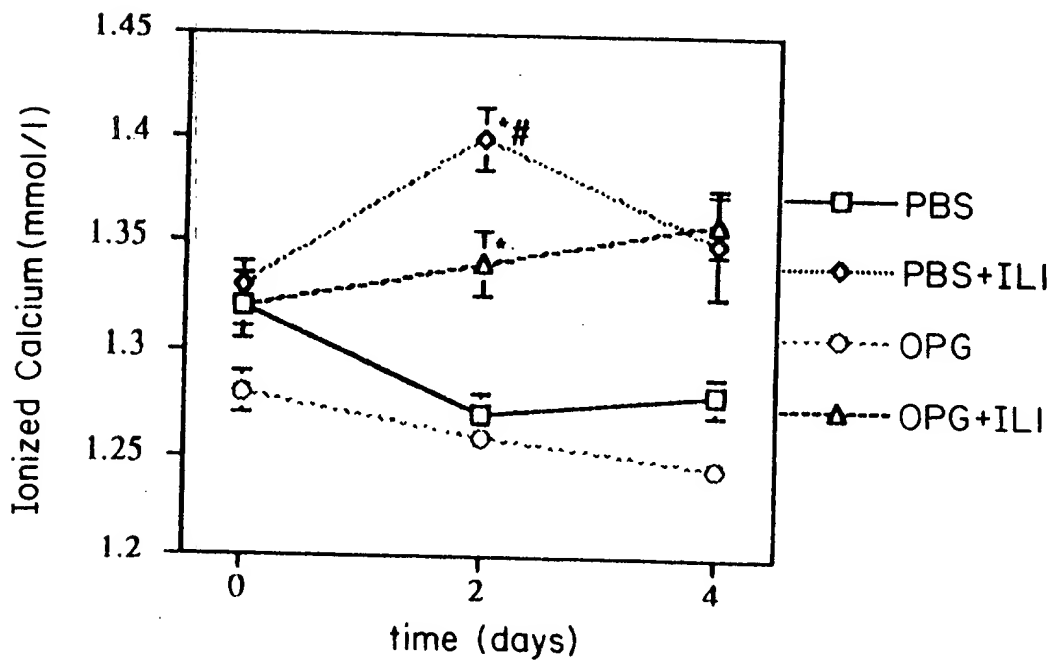


FIG.22B



\* Different to PBS,  $p < 0.05$

# Different to OPG + ILI,  $p < 0.05$



FIG.23A

PBS/PBS



FIG.23B

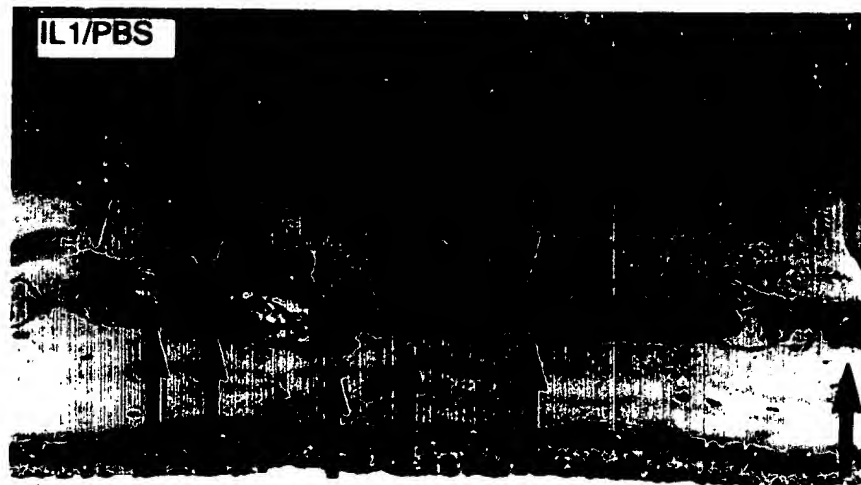


FIG.23C

PBS/OPG



FIG.23D



FIG. 24B

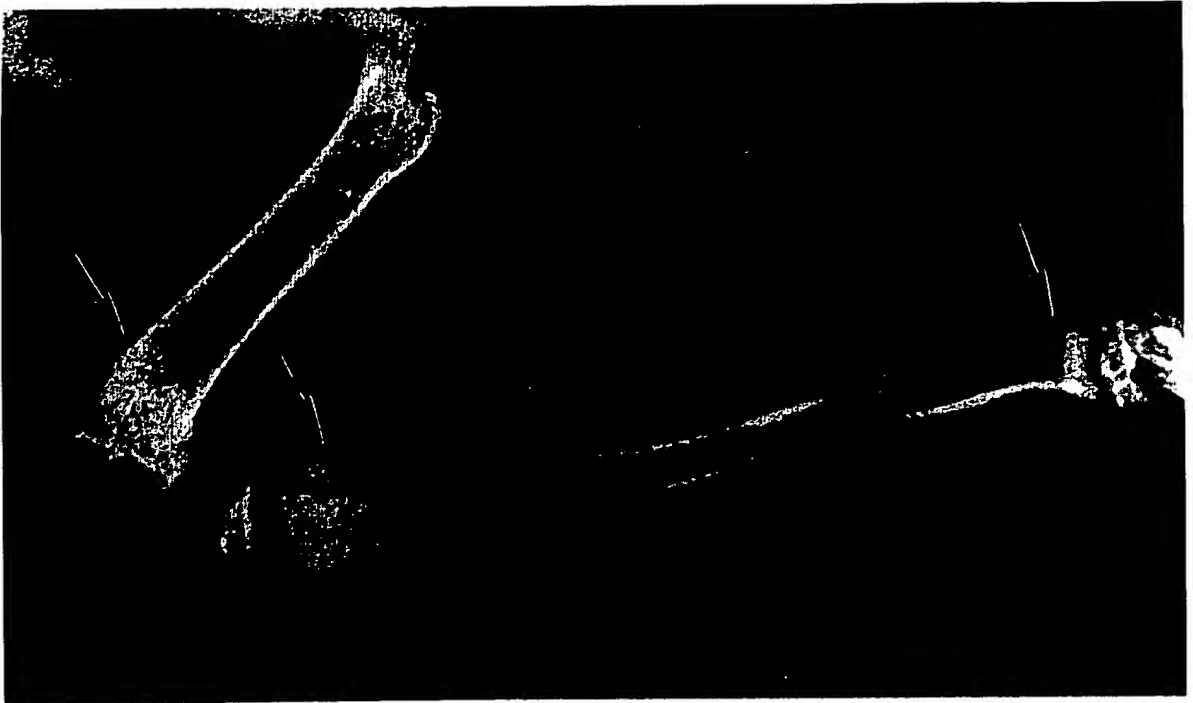
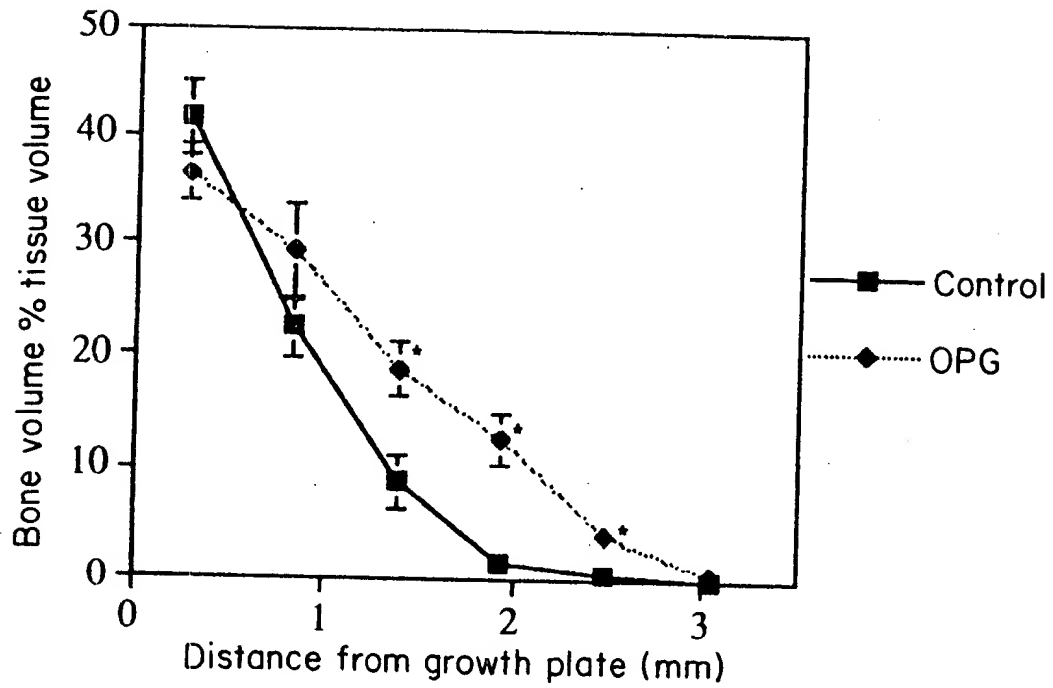


FIG. 24A



TITLE: COMBINATION THERAPY FOR CONDITIONS  
LEADING TO BONE LOSS  
INVENTORS: Boyle, et al.  
APPLN. NO: A-378CIP5

FIG.25



\* Different to control  $p < 0.01$

**FIG. 26A**



**FIG. 26B**



FIG.27

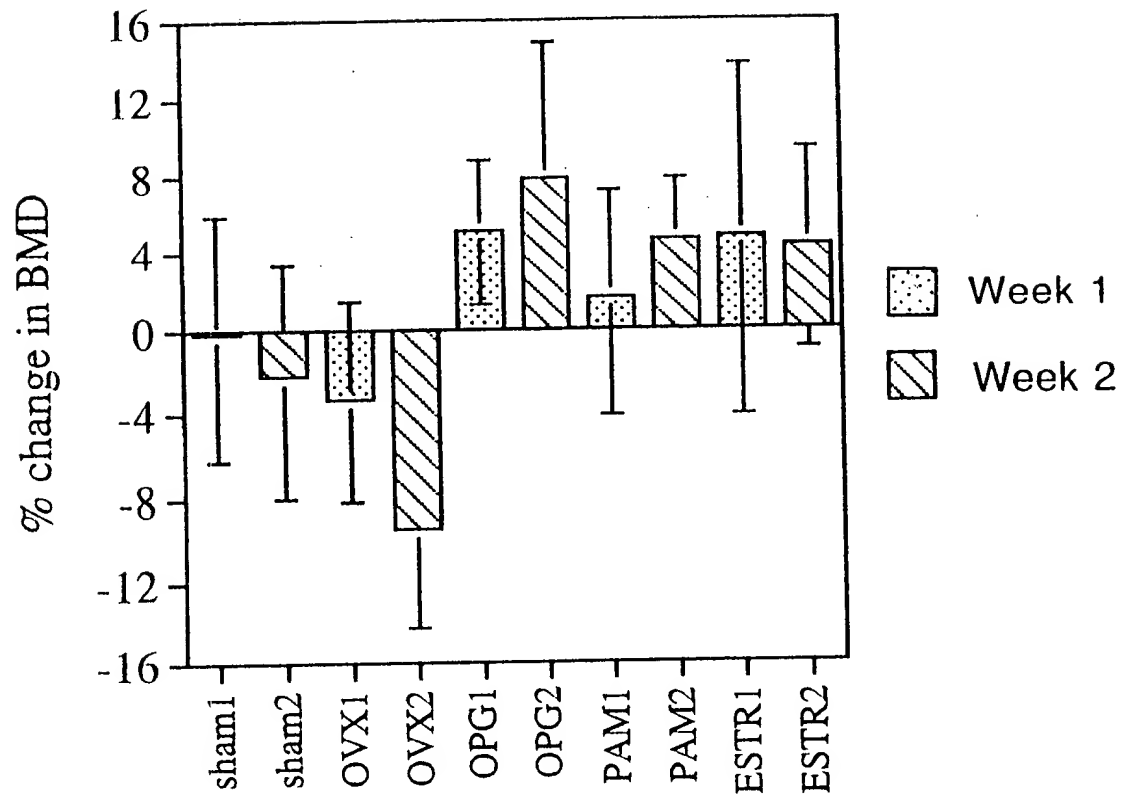
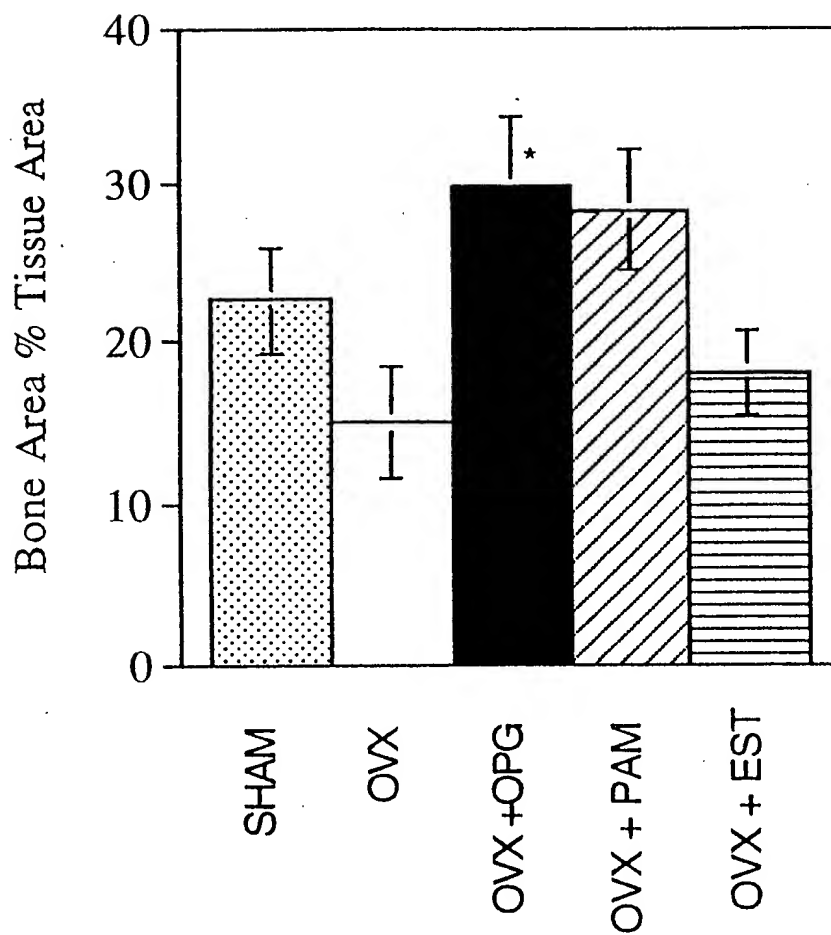


FIG.28



\* Different to OVX  $p < 0.05$

TITLE: COMBINATION THERAPY FOR CONDITIONS  
LEADING TO BONE LOSS  
INVENTORS: Boyle, et al.  
APPLN. NO: A-378CIP5

## FIG. 29A

DraIII

1 CATGGGAAATGTCAGAGTGGAGAACCACACCGAGTGCCACTGCAGCACTTGTTATTATCA 60  
GTACCCCTTTACAGTCTCACCTCTTGGTGTGGCTCACGGTGACGTCGTGAACAATAATAGT  
61 CAAATCCTAATAGTTTGCAGTGGGCCTTGCTGATGATGGCTGACTTGCTCAAAGGAAAA 120  
GTTTAGGATTATCAAACGTCACCCGGAACGACTACTACCGACTGAACGAGTTTTCCTTTT  
121 TTAATTTGTCCAGTGTCTATGGCTTTGTGAGATAAAACCCTCCTTTTCCTTGCCATACCA 180  
AATTAAACAGGTACAGATACCGAAACACTCTATTTTGGGAGGAAAAGGAACGGTATGGT  
181 TTTTAAACCTGCTTTGAGAATATACTGCAGCTTTATTGCTTTTCTCCTTATCCTACAATA 240  
AAAAATTGGACGAAACTCTTATATGACGTCGAAATAACGAAAAGAGGAATAGGATGTTAT  
241 TAATCAGTAGTCTTGATCTTTTCATTGGAATGAAATATGGCATTTAGCATGACCATAAA 300  
ATTAGTCATCAGAACTAGAAAAGTAAACCTTACTTTATACCGTAAATCGTACTGGTATTT  
301 AAGCTGATTCCACTGGAAATAAAGTCTTTTAAATCATCACTCTATCACTGAATTCTAATT 360  
TTCGACTAAGGTGACCTTTATTTTCAGAAAATTTAGTAGTGAGATAGTGACTTAAGATTAA  
361 TTTTCTGAAAAGTTTCAAGCCAGTTACTTTTGATAGGATTAACGGAAGGGAGTGAGCCAG 420  
AAAAGACTTTTCAAAGTTCGGTCAATGAAAACATCCTAATTGCCTTCCTCACTCGGTC

XcmI

421 TGGGTGAGGTGGGTTC CATGTAGTCAATGGCCTAATACTGGAGAATCTTATTCTAACCA 480  
ACCCACTCCACCCAAGGGTACATCAGTTACCGGATTATGACCTCTTAGAATAAGATTGGT  
481 AGCCTTCCAGAGCAAGCTGTGAGCCCCCTCAGACAGTGGGCTACTCATGAGACAGTCCATT 540  
TCGGAAGGTCTCGTTCGACACTCGGGGAGTCTGTCACCCGATGAGTACTCTGTCAGGTAA  
541 GGGGTAAAGGAAGAAAATATAACTTCTATTTCTATTTCATTTGCACATTGTCTTTAGATGC 600  
CCCCATTTCTTCTTTTATATTGAAGATAAAGATAAGTAAACGTGTAACAGAAATCTACG  
601 CCATTTGGGTGAGTTTTATAGAAGTACAGCTACATTAATAAATAAGAACTGATAATAGATA 660  
GGTAAACCCACTCAAATATCTTCATGTCGATGTAATTTTTTATCTTGACTATTATCTAT



TITLE: COMBINATION THERAPY FOR CONDITIONS  
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APPLN. NO: A-378CIP5

## FIG. 29B

```
AGGCTTTAAAAAACTTCATTCATCACCAGTTTGTCAAGATTCCATTTCAAAGTGAAAAA
661 -----+-----+-----+-----+-----+-----+ 720
TCCGAAATTTTTTTGAAGTAAGTAGTGGTCAAACAGTTCTAAGGTAAAGTTTCACTTTTT

CCAATTTCTAACGGGTGGTAAACACAGCAGATGGCAGGGTGAAAAATTAAAGTGAGTGC
721 -----+-----+-----+-----+-----+-----+ 780
GGTTAAAGATTGCCCAACCATTGTGTGCTGTACCGTCCCCTTTTAAATTTCACTCACG

ATGTACCTTTAAAGAAACACTGAAATGCACACACATTACTTAACCTGCTCATTCTTTAT
781 -----+-----+-----+-----+-----+-----+ 840
TACATGGAAATTTCTTTGTGACTTTACGTGTGTGTAATGAATTGGACGAGTAAGTAAATA

TTACATATAGTCTTGGGTGTACAAAATTTAGAAATAAATACATATGGGGGCGGGGCCTTA
841 -----+-----+-----+-----+-----+-----+ 900
AATGTATATCAGAACCCACATGTTTTAAATCTTTATTTATGTATACCCCCGCCCCGGAAT

GCTGCACAAATAGGATGCGCGGCGGGCCTTGGTAGGGGCGGAGCCTTAGCTGCACAAATA
901 -----+-----+-----+-----+-----+-----+ 960
CGACGTGTTTATCCTACGCGCCGCGCCGAACCATCCCCGCCTCGGAATCGACGTGTTTAT

GGATGCGCGGCGGGCCTTGGTGGGGGCGGGGCCCTAAGCTGCGCAAGTGGTACACAGCTCA
961 -----+-----+-----+-----+-----+-----+ 1020
CCTACGCGCCGCGCCGGAACCAACCCCGCCCGGATTCGACGCGTTCACCATGTGTGAGT

GGGCTGCGATTTTCGCGCCAACTTGACGGCAATCCTAGCGTGAAGGCTGGTAGGATTTTA
1021 -----+-----+-----+-----+-----+-----+ 1080
CCCGACGCTAAAGCGCGGTTTGAAGTGCCTTAGGATCGCACTTCCGACCATCCTAAAAT

TCCCCGCTGCCATCATGGTTCGACCATTGAACTGCATCGTCGCGTGTCCCAAAATATGG
1081 -----+-----+-----+-----+-----+-----+ 1140
AGGGGCGACGGTAGTACCAAGCTGGTAACTTGACGTAGCAGCGGCACAGGGTTTATACC

GGATTGGCAAGAACGGAGACCTACCCTGGCCTCCGCTCAGGAACGAGTTCAAGTACTTCC
1141 -----+-----+-----+-----+-----+-----+ 1200
CCTAACC GTTCTTG CCTCTGGATGGGACCGGAGGCGAGTCTTGCTCAAGTTCATGAAGG

AAAGAATGACCACAACCTCTTCAGTGGAAGGTAAACAGAATCTGGTGATTATGGGTAGGA
1201 -----+-----+-----+-----+-----+-----+ 1260
TTTCTTACTGGTGTTGGAGAAGTCACCTTCCATTTGTCTTAGACCACTAATACCCATCCT

AAACCTGGTTCCTCATTCCTGAGAAGAATCGACCTTTAAAGGACAGAATTAATATAGTTC
1261 -----+-----+-----+-----+-----+-----+ 1320
TTTGGACCAAGAGGTAAGGACTCTTCTTAGCTGGAAATTTCTGTCTTAATTATATCAAG
```

SacI

BstXI

TCAGTAGAGAACTCAAAGAACCACCACGAGGAGCTCATTTTCTTGCCAAAAGTTTGATG

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LEADING TO BONE LOSS  
INVENTORS: Boyle, et al.  
APPLN. NO: A-378CIP5

## FIG. 29C

AflII  
|  
ATGCCTTAAGACTTATTGAACAACCGGAATTGGCAAGTAAAGTAGACATGGTTTGGATAG  
1381 -----+-----+-----+-----+-----+-----+ 1440  
TACGGAATTCTGAATAACTTGTGGCCTTAACCGTTCATTTTCATCTGTACCAAACCTATC  
  
TCGGAGGCAGTTCTGTTTACCAGGAAGCCATGAATCAACCAGGCCACCTCAGACTCTTTG  
1441 -----+-----+-----+-----+-----+-----+ 1500  
AGCCTCCGTCAAGACAAATGGTCCTTCGGTACTTAGTTGGTCCGGTGGAGTCTGAGAAAC  
  
TGACAAGGATCATGCAGGAATTTGAAAGTGACACGTTTTTCCCAGAAATTGATTTGGGGA  
1501 -----+-----+-----+-----+-----+-----+ 1560  
ACTGTTCCCTAGTACGTCCTTAACTTTCACTGTGCAAAAAGGGTCTTTAACTAAACCCCT  
  
AATATAAACTTCTCCCAGAATACCCAGGCGTCCTCTCTGAGGTCCAGGAGGAAAAAGGCA  
1561 -----+-----+-----+-----+-----+-----+ 1620  
TTATATTTGAAGAGGGTCTTATGGGTCCGCAGGAGAGACTCCAGGTCCTCCTTTTTCCGT  
  
TCAAGTATAAGTTTGAAGTCTACGAGAAGAAAGACTAACAGGAAGATGCTTTCAAGTTCT  
1621 -----+-----+-----+-----+-----+-----+ 1680  
AGTTCATATTCAAACCTTCAGATGCTCTTCTTTCTGATTGTCCTTCTACGAAAGTTCAAGA  
  
BglII  
|  
CTGCTCCCCTCCTAAAGCTATGCATTTTTATAAGACCATGGGACTTTTGCTGGCTTTAGA  
1681 -----+-----+-----+-----+-----+-----+ 1740  
GACGAGGGGAGGATTTGATACGTAATAAATATTCTGGTACCCTGAAAACGACCGAAATCT  
  
TCTGAAACACTGAAATTGTCTGCTTCTCATCTTCAGTGAGATTCCAAAGGATAGTACAGT  
1741 -----+-----+-----+-----+-----+-----+ 1800  
AGACTTTGTGACTTTAACAGACGAAGAGTAGAAGTCACTCTAAGGTTTCCTATCATGTCA  
  
GACAGAACAAGAATAGGCACTCTCTACAAAAAAGAAAGAAAAAACTAAGTAATAGCAA  
1801 -----+-----+-----+-----+-----+-----+ 1860  
CTGTCTTGTTCTTATCCGTGAGAGATGTTTTTTTCTTTCTTTTGTATTCAATATCGTT  
  
GCATAATAGCTACTGTTAAGAACTCAGAGATAATGAATTGAGAATGGATACTGCTTGAAA  
1861 -----+-----+-----+-----+-----+-----+ 1920  
CGTATTATCGATGACAATTCTTGAGTCTCTATTACTTAACTCTTACCTATGACGAACTTT  
  
TGAAAATTTAATAAGTTAGAACTAACTTTATAAAAAATAAAAAAATGAGCATTAAAAAA  
1921 -----+-----+-----+-----+-----+-----+ 1980  
ACTTTTAAATTATTCAATCTTTGATTGAAATATTTTTATTTTTTACTCGTAATTTTTT  
  
NheI  
|  
AAAAAAAAAAAAAAAAAAAAACCCCCCCCCCCCCCTGCAGCCAAGCTAGCTTGGAAATC  
1981 -----+-----+-----+-----+-----+-----+ 2040

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LEADING TO BONE LOSS  
INVENTORS: Boyle, et al.  
APPLN. NO: A-378CIP5

## FIG. 29D

BspLU11I

AGGGGATAACGCAGGAAAGAACATGTGAGCAAAAGGCCAGCAAAAGGCCAGGAACCGTAA  
2041 -----+-----+-----+-----+-----+-----+ 2100  
TCCCCTATTGCGTCCTTTCTTGTACACTCGTTTTCCGGTCGTTTTCCGGTCCTTGGCATT  
  
AAAGGCCGCGTTGCTGGCGTTTTTCCATAGGCTCCGCCCCCTGACGAGCATCACAAAAA  
2101 -----+-----+-----+-----+-----+-----+ 2160  
TTTCCGGCGCAACGACCGCAAAAAGGTATCCGAGGCGGGGGGACTGCTCGTAGTGTTTTT  
  
TCGACGCTCAAGTCAGAGGTGGCGAAACCCGACAGGACTATAAAGATACCAGGCGTTTCC  
2161 -----+-----+-----+-----+-----+-----+ 2220  
AGCTGCGAGTTCAGTCTCCACCGCTTTGGGCTGTCCTGATATTTCTATGGTCCGCAAAGG  
  
CCCTGGAAGCTCCCTCGTGCGCTCTCCTGTTCCGACCCTGCCGCTTACCGGATACCTGTC  
2221 -----+-----+-----+-----+-----+-----+ 2280  
GGGACCTTCGAGGGAGCACGCGAGAGGACAAGGCTGGGACGGCGAATGGCCTATGGACAG  
  
CGCCTTTCTCCCTTCGGGAAGCGTGGCGCTTTCTCATAGCTCACGCTGTAGGTATCTCAG  
2281 -----+-----+-----+-----+-----+-----+ 2340  
GCGGAAAGAGGGAAGCCCTTCGCACCGCGAAAGAGTATCGAGTGCGACATCCATAGAGTC  
  
TTCGGTGTAGGTCGTTTCGCTCCAAGCTGGGCTGTGTGCACGAACCCCCCGTTTACGCCCGA  
2341 -----+-----+-----+-----+-----+-----+ 2400  
AAGCCACATCCAGCAAGCGAGGTTGACCCGACACACGTGCTTGGGGGGCAAGTCGGGCT  
  
CCGCTGCGCCTTATCCGGTAACTATCGTCTTGAGTCCAACCCGGTAAGACACGACTTATC  
2401 -----+-----+-----+-----+-----+-----+ 2460  
GGCGACGCGGAATAGGCCATTGATAGCAGAACTCAGGTTGGGCCATTCTGTGCTGAATAG  
  
GCCACTGGCAGCAGCCACTGGTAACAGGATTAGCAGAGCGAGGTATGTAGGCGGTGCTAC  
2461 -----+-----+-----+-----+-----+-----+ 2520  
CGGTGACCGTCGTCGGTGACCATTGTCCTAATCGTCTCGCTCCATACATCCGCCACGATG  
  
AGAGTTCTTGAAGTGGTGGCCTAACTACGGCTACACTAGAAGGACAGTATTTGGTATCTG  
2521 -----+-----+-----+-----+-----+-----+ 2580  
TCTCAAGAACTTCACCACCGGATTGATGCCGATGTGATCTTCCTGTCATAAACCATAGAC  
  
CGCTCTGCTGAAGCCAGTTACCTTCGGAAAAAGAGTTGGTAGCTCTTGATCCGGCAAACA  
2581 -----+-----+-----+-----+-----+-----+ 2640  
GCGAGACGACTTCGGTCAATGGAAGCCTTTTTCTCAACCATCGAGAACTAGGCCGTTTGT

HgiEII

AACCACCGCTGGTAGCGGTGGTTTTTTTTGTTTGCAAGCAGCAGATTACGCGCAGAAAAA  
2641 -----+-----+-----+-----+-----+-----+ 2700  
TTGGTGGCGACCATCGCCACCAAAAAACAAACGTTTCGTGCTCTAATGCGCGTCTTTTTT  
  
AGGATCTCAAGAAGATCCTTTGATCTTTTCTACGGGGTCTGACGCTCAGTGGAACGAAAA  
2701 -----+-----+-----+-----+-----+-----+ 2760

TITLE: COMBINATION THERAPY FOR CONDITIONS  
LEADING TO BONE LOSS  
INVENTORS: Boyle, et al.  
APPLN. NO: A-378CIP5

## FIG. 29E

```
CTCACGTTAAGGGATTTTGGTCATGAGATTATCAAAAAGGATCTTCACCTAGATCCTTTT
2761 -----+-----+-----+-----+-----+-----+-----+ 2820
GAGTGCAATTCCCTAAAACCAGTACTCTAATAGTTTTTTCCTAGAAGTGGATCTAGGAAAA

AAATTAAAAATGAAGTTTTTAAATCAATCTAAAGTATATATGAGTAACTTGGTCTGACAG
2821 -----+-----+-----+-----+-----+-----+-----+ 2880
TTTAATTTTTTACTTCAAATTTAGTTAGATTTTCATATATACTCATTTGAACCAGACTGTC

TTACCAATGCTTAATCAGTGAGGCACCTATCTCAGCGATCTGTCTATTTTCGTTTCATCCAT
2881 -----+-----+-----+-----+-----+-----+-----+ 2940
AATGGTTACGAATTAGTCACTCCGTGGATAGAGTCGCTAGACAGATAAAGCAAGTAGGTA

AGTTGCCTGACTCCCCGTCGTGTAGATAACTACGATACGGGAGGGCTTACCATCTGGCCC
2941 -----+-----+-----+-----+-----+-----+-----+ 3000
TCAACGGACTGAGGGGCAGCACATCTATTGATGCTATGCCCTCCCGAATGGTAGACCGGG

CAGTGCTGCAATGATACCGCGAGACCCACGCTCACC GGCTCCAGATTTATCAGCAATAAA
3001 -----+-----+-----+-----+-----+-----+-----+ 3060
GTCACGACGTTACTATGGCGCTCTGGGTGCGAGTGGCCGAGGTCTAAATAGTCGTTATTT

CCAGCCAGCCGGAAGGGCCGAGCGCAGAAGTGGTCCTGCAACTTTATCCGCCCTCCATCCA
3061 -----+-----+-----+-----+-----+-----+-----+ 3120
GGTCGGTCGGCCTTCCCGGCTCGCGTCTTCACCAGGACGTTGAAATAGGCGGAGGTAGGT

GTCTATTAATTGTTGCCGGGAAGCTAGAGTAAGTAGTTCGCCAGTTAATAGTTTGCGCAA
3121 -----+-----+-----+-----+-----+-----+-----+ 3180
CAGATAATTAACAACGGCCCTTCGATCTCATTCATCAAGCGGTCAATTATCAAACGCGTT

CGTTGTTGCCATTGCTGCAGGCATCGTGGTGTACGCTCGTCGTTTGGTATGGCTTCATT
3181 -----+-----+-----+-----+-----+-----+-----+ 3240
GCAACAACGGTAACGACGTCCGTAGCACCACAGTGCGAGCAGCAAACCATAACCGAAGTAA

CAGCTCCGGTTCCCAACGATCAAGGCGAGTTACATGATCCCCCATGTTGTGCAAAAAAGC
3241 -----+-----+-----+-----+-----+-----+-----+ 3300
GTCGAGGCCAAGGGTTGCTAGTTCCGCTCAATGTACTAGGGGGTACAACACGTTTTTTTCG

                                EaeI
                                |
          PvuI                GdiII
          |                    |
GGTTAGCTCCTTCGGTCCTCCGATCGTTGTCAGAAGTAAGTTGGCCGCAGTGTTATCACT
3301 -----+-----+-----+-----+-----+-----+-----+ 3360
CCAATCGAGGAAGCCAGGAGGCTAGCAACAGTCTTCATTCAACCGGCGTCACAATAGTGA

CATGGTTATGGCAGCACTGCATAATTCTCTTACTGTCATGCCATCCGTAAGATGCTTTTC
3361 -----+-----+-----+-----+-----+-----+-----+ 3420
GTACCAATACCGTCGTGACGTATTAAGAGAATGACAGTACGGTAGGCATTCTACGAAAAG

                                BcgI
                                |
TGTGACTGGTGAGTACTCAACCAAGTCATTCTGAGAATAGTGTATGCGGCGACCGAGTTG
```

TITLE: COMBINATION THERAPY FOR CONDITIONS  
LEADING TO BONE LOSS  
INVENTORS: Boyle, et al.  
APPLN. NO: A-378CIP5

## FIG. 29F

```
CTCTTGCCCGGCGTCAACACGGGATAATACCGCGCCACATAGCAGAACTTTAAAAGTGCT
3481 -----+-----+-----+-----+-----+-----+ 3540
GAGAACGGGCCGCGAGTTGTGCCCTATTATGGCGCGGTGTATCGTCTTGAAATTTTCACGA

CATCATTGAAAACGTTCTTCGGGGCGAAAACCTCTCAAGGATCTTACCGCTGTTGAGATC
3541 -----+-----+-----+-----+-----+-----+ 3600
GTAGTAACCTTTTGCAAGAAGCCCCGCTTTTGAGAGTTCCTAGAATGGCGACAACCTCTAG

CAGTTCGATGTAACCCACTCGTGCACCCAACTGATCTTCAGCATCTTTTACTTTCACCAG
3601 -----+-----+-----+-----+-----+-----+ 3660
GTCAAGCTACATTGGGTGAGCACGTGGGTGACTAGAAGTCGTAGAAAATGAAAGTGGTC

CGTTTCTGGGTGAGCAAAAACAGGAAGGCAAAATGCCGCAAAAAGGGAATAAGGGCGAC
3661 -----+-----+-----+-----+-----+-----+ 3720
GCAAAGACCCACTCGTTTTTGTCTTCCGTTTTACGGCGTTTTTCCCTTATTCCTCGCTG

SspI
|
ACGGAAATGTTGAATACTCATACTCTTCCTTTTCAATATTATTGAAGCATTTATCAGGG
3721 -----+-----+-----+-----+-----+-----+ 3780
TGCCTTTACAACCTTATGAGTATGAGAAGGAAAAAGTTATAATAACTTCGTAAATAGTCCC

TTATTGTCTCATGAGCGGATACATATTTGAATGTATTTAGAAAAATAAACAAATAGGGGT
3781 -----+-----+-----+-----+-----+-----+ 3840
AATAACAGAGTACTCGCCTATGTATAAACTTACATAAATCTTTTATTTGTTTATCCCCA

TCCGCGCACATTTCCCCGAAAAGTGCCACCTGACGTCTAAGAAACCATTATTATCATGAC
3841 -----+-----+-----+-----+-----+-----+ 3900
AGGCGCGTGTAAGGGGGCTTTTCACGGTGGACTGCAGATTCTTTGGTAATAATAGTACTG

ATTAACCTATAAAAATAGGCGTATCACGAGGCCCTTTTCGTCTTCAAGAATTCCTGTGGA
3901 -----+-----+-----+-----+-----+-----+ 3960
TAATTGGATATTTTATCCGCATAGTGCTCCGGGAAAGCAGAAGTTCTTAAGGGACACCT

ATGTGTGTCAGTTAGGGTGTGGAAAGTCCCCAGGCTCCCCAGCAGGCAGAAGTATGCAAA
3961 -----+-----+-----+-----+-----+-----+ 4020
TACACACAGTCAATCCCACACCTTTCAGGGGTCCGAGGGGTCGTCCGTCTTCATACGTTT

GCATGCATCTCAATTAGTCAGCAACCAGGTGTGGAAAGTCCCCAGGCTCCCCAGCAGGCA
4021 -----+-----+-----+-----+-----+-----+ 4080
CGTACGTAGAGTTAATCAGTCGTTGGTCCACACCTTTCAGGGGTCCGAGGGGTCGTCCGT

GAAGTATGCAAAGCATGCATCTCAATTAGTCAGCAACCATAGTCCCGCCCCCTAACTCCGC
4081 -----+-----+-----+-----+-----+-----+ 4140
CTTCATACGTTTCGTACGTAGAGTTAATCAGTCGTTGGTATCAGGGCGGGGATTGAGGCG

CCATCCCGCCCCCTAACTCCGCCCAGTTCGCCCCATTCTCCGCCCCATGGCTGACTAATTT
4141 -----+-----+-----+-----+-----+-----+ 4200
```

TITLE: COMBINATION THERAPY FOR CONDITIONS  
LEADING TO BONE LOSS  
INVENTORS: Boyle, et al.  
APPLN. NO: A-378CIP5

## FIG. 29G

SfiI  
|  
TTTTTATTTATGCAGAGGCCGAGGCCGCTCGGCCCTCTGAGCTATTCCAGAAGTAGTGAG  
4201 -----+-----+-----+-----+-----+-----+ 4260  
AAAAATAAATACGTCTCCGGCTCCGGCGGAGCCGGAGACTCGATAAGGTCTTCATCACTC

AvrII  
|  
GAGGCTTTTTTGGAGGCCTAGGCTTTTGCAAAAAGCTGGTCGAGGCTCGCATCTCTCCTT  
4261 -----+-----+-----+-----+-----+-----+ 4320  
CTCCGAAAAAACCTCCGGATCCGAAACGTTTTTCGACCAGCTCCGAGCGTAGAGAGGAA  
  
CACGCGCCCGCCGCCCTACCTGAGGCCGCCATCCACGCCGGTTGAGTCGCGTTCTGCCGC  
4321 -----+-----+-----+-----+-----+-----+ 4380  
GTGCGCGGGCGGCGGGATGGACTCCGGCGGTAGGTGCGGCCAACTCAGCGCAAGACGGCG  
  
CTCCCGCCTGTGGTGCTCCTGAACTGCGTCCGCCGTCTAGGTAAGTTTAAAGCTCAGGT  
4381 -----+-----+-----+-----+-----+-----+ 4440  
GAGGGCGGACACCACGGAGGACTTGACGCAGGCGGCAGATCCATTCAAATTCGAGTCCA

NgoAIV  
|  
CGAGACCGGGCCTTTGTCCGGCGCTCCCTTGGAGCCTACCTAGACTCAGCCGGCTCTCCA  
4441 -----+-----+-----+-----+-----+-----+ 4500  
GCTCTGGCCCCGAAACAGGCCGCGAGGGAACCTCGGATGGATCTGAGTCGGCCGAGAGGT  
  
CGCTTTGCCTGACCCTGCTTGCTCAACTCTACGTCTTTGTTTCGTTTTCTGTTCTGCGCC  
4501 -----+-----+-----+-----+-----+-----+ 4560  
GCGAAACGGACTGGGACGAACGAGTTGAGATGCAGAAACAAAGCAAAAGACAAGACGCGG

HpaI  
|  
GTTACAGATCCGTCGAGGAACTGAAAAACCAGAAAGTTAACTGGTAAGTTTAGTCTTTTT  
4561 -----+-----+-----+-----+-----+-----+ 4620  
CAATGTCTAGGCAGCTCCTTGACTTTTTTGGTCTTCAATTGACCATTCAAATCAGAAAAA

Psp5II BamHI  
| |  
GTCTTTTATTTTCAAGTCCCGGATCCGGTGGTGGTGCAATCAAAGAACTGCTCCTCAGTG  
4621 -----+-----+-----+-----+-----+-----+ 4680  
CAGAAAATAAAGTCCAGGGCCTAGGCCACCACCACGTTTAGTTTCTTGACGAGGAGTCAC  
  
GATGTTGCCTTTACTTCTAGGCCTGTACGGAAGTGTTACTTCTGCTCTAAAAGCTGCTGC  
4681 -----+-----+-----+-----+-----+-----+ 4740  
CTACAACGGAAATGAAGATCCGGACATGCCTTCACAATGAAGACGAGATTTTCGACGACG

HindIII XbaI  
| |  
AACAGCTTCTAGACCACCATGAACAAGTTGCTGTGCTGCGCGCTCGTGTTTCTGGACAT  
4741 -----+-----+-----+-----+-----+-----+ 4800  
TTGTTCTGAAGATCTGGTGGTACTTGTTCACGACACGACGCGGAGCACAAAGACCTGTA

BssHII  
|

**FIG. 29H**

CTCCATTAAGTGGACCAACGTTTCCTCCAAAGTACCTTCATTATGACGAAGA  
4801 -----+-----+-----+-----+-----+-----+-----+ 4860  
GAGGTAATTCACCTGGTGGGTCCTTTGCAAAGGAGGTTTCATGGAAGTAATACTGCTTCT  
b S I K W T T Q E T F P P K Y L H Y D E E -

KpnI  
|

AACCTCTCATCAGCTGTTGTGTGACAAATGTCTCCTGGTACCTACCTAAACAACACTG  
4861 -----+-----+-----+-----+-----+-----+ 4920  
TTGGAGAGTAGTCGACAACACACTGTTTACAGGAGGACCATGGATGGATTTTGTGTGAC  
b T S H Q L L C D K C P P G T Y L K Q H C -

TACAGCAAAGTGAAGACCGTGTGCGCCCCTTGCCCTGACCACTACTACACAGACAGCTG  
4921 -----+-----+-----+-----+-----+-----+ 4980  
ATGTCGTTTCACCTTCTGGCACACGCGGGGAACGGGACTGGTGATGATGTGTCTGTCTGAC  
b T A K W K T V C A P C P D H Y Y T D S W -

GCACACCAGTGACGAGTGTCTATACTGCAGCCCCGTGTGCAAGGAGCTGCAGTACGTCAA  
4981 -----+-----+-----+-----+-----+-----+ 5040  
CGTGTGGTCACTGCTCACAGATATGACGTCGGGGCACACGTTCCCTCGACGTCATGCAGTT  
b H T S D E C L Y C S P V C K E L Q Y V K -

RleAI BsmI  
| |

GCAGGAGTGCAATCGCACCCACAACCGCGTGTGCGAATGCAAGGAAGGGCGCTACCTTGA  
5041 -----+-----+-----+-----+-----+-----+ 5100  
CGTCCTCACGTTAGCGTGGGTGTTGGCGCACACGCTTACGTTCCCTCCCGCGATGGAAGT  
b Q E C N R T H N R V C E C K E G R Y L E -

GATAGAGTTCTGCTTGAAACATAGGAGCTGCCCTCCTGGATTTGGAGTGGTGCAAGCTGG  
5101 -----+-----+-----+-----+-----+-----+ 5160  
CTATCTCAAGACGAAGTTTGTATCCTCGACGGGAGGACCTAAACCTCACCACGTTTCGACC  
b I E F C L K H R S C P P G F G V V Q A G -

BsmBI  
|

AACCCAGAGCGAAATACAGTTTGCAAAGATGTCCAGATGGGTTCTTCTCAAATGAGAC  
5161 -----+-----+-----+-----+-----+-----+ 5220  
TTGGGGTCTCGCTTTATGTCAAACGTTTCTACAGGTCTACCCAAGAAGAGTTTACTCTG  
b T P E R N T V C K R C P D G F F S N E T -

GTCATCTAAAGCACCCCTGTAGAAACACACAAATTGCAGTGTCTTTGGTCTCCTGCTAAC  
5221 -----+-----+-----+-----+-----+-----+ 5280  
CAGTAGATTTTCGTGGGACATCTTTTGTGTGTTTAAACGTACAGAAACCAGAGGACGATTG  
b S S K A P C R K H T N C S V F G L L L T -

BspEI  
|

TCAGAAAGGAAATGCAACACACGACAACATATGTTCCGGAAACAGTGAATCAACTCAAAA  
5281 -----+-----+-----+-----+-----+-----+ 5340

[illegible]



TITLE: COMBINATION THERAPY FOR CONDITIONS  
LEADING TO BONE LOSS  
INVENTORS: Boyle, et al.  
APPLN. NO: A-378CIP5

## FIG. 29J

AarI

CTCCGACGGCTCCTTCTTCCTCTACAGCAAGCTCACCGTGGACAAGAGCAGGTGGCAGCA  
5881 -----+-----+-----+-----+-----+-----+ 5940  
GAGGCTGCCGAGGAAGAAGGAGATGTCGTTGAGTGGCACCTGTTCTCGTCCACCGTCGT  
b S D G S F F L Y S K L T V D K S R W Q Q -

SapI

GGGGAACGTCTTCTCATGCTCCGTGATGCATGAGGCTCTGCACAACCACTACACGCAGAA  
5941 -----+-----+-----+-----+-----+ 6000  
CCCCTTGCAGAAGAGTACGAGGCACTACGTACTCCGAGACGTGTTGGTGATGTGCGTCTT  
b G N V F S C S V M H E A L H N H Y T Q K -

GAGCCTCTCCCTGTCTCCGGGTAAATGATAACTCGAC  
6001 -----+-----+-----+-----+ 6037  
CTCGGAGAGGGACAGAGGCCCATTTACTATTGAGCTG  
b S L S L S P G K \* \*

FIG. 30A-1

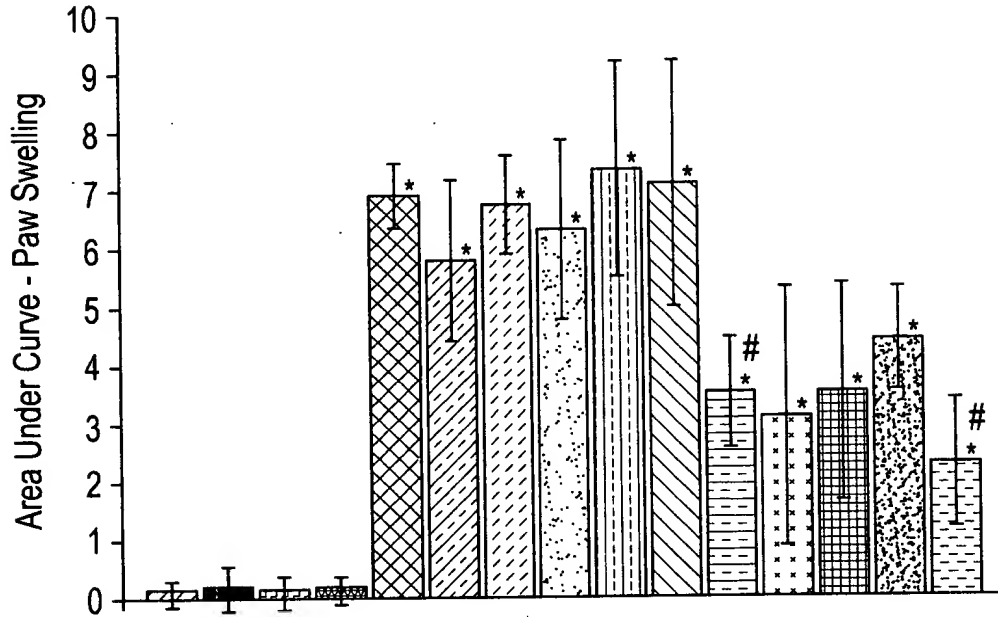
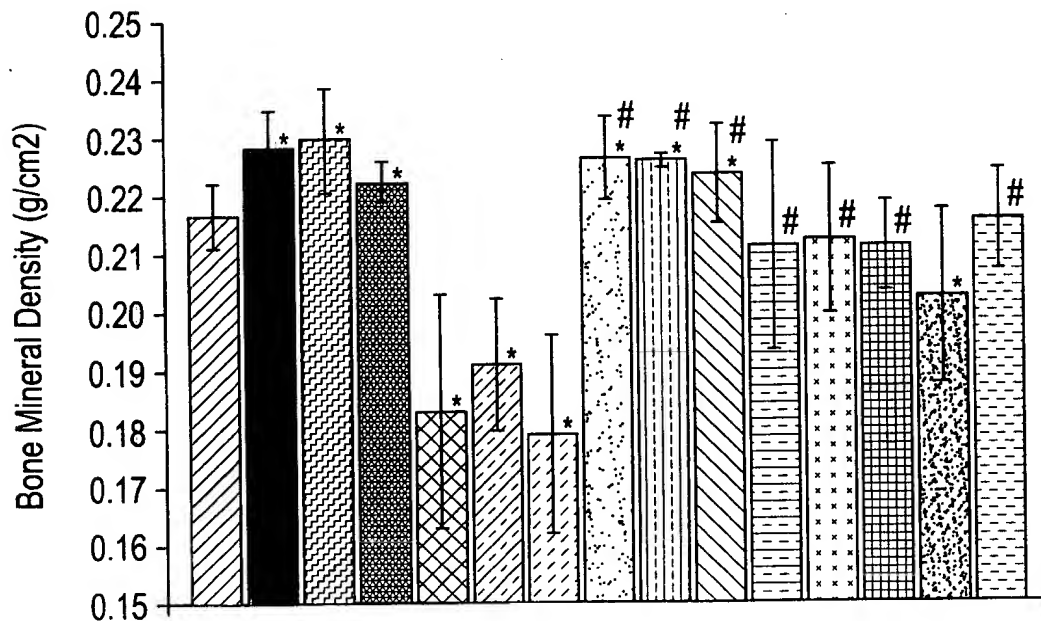


FIG. 30A-2



- |                                   |                                       |
|-----------------------------------|---------------------------------------|
| Normal (NT)                       | AdA + 1.0 mg/kg OPG-Fc (s.c.)         |
| Normal + 4 mg/kg OPG-Fc (s.c.)    | AdA + 0.25 mg/kg OPG-Fc (s.c.)        |
| Normal + 1.0 mg/kg OPG-Fc (s.c.)  | 15.0 mg/kg/hr IL-1ra (2ML1)           |
| Normal + 0.25 mg/kg OPG-Fc (s.c.) | 5.0 mg/kg/hr IL-1ra (2ML1)            |
| AdA Control                       | 1.0 mg/kg/hr IL-1ra (2ML1)            |
| AdA + CSEP (2ML1)                 | 0.2 mg/kg/hr IL-1ra (2ML1)            |
| AdA + OPG Placebo (s.c.)          | AdA + 0.07 mg/kg Dexamethasone (s.c.) |

FIG. 30B-1

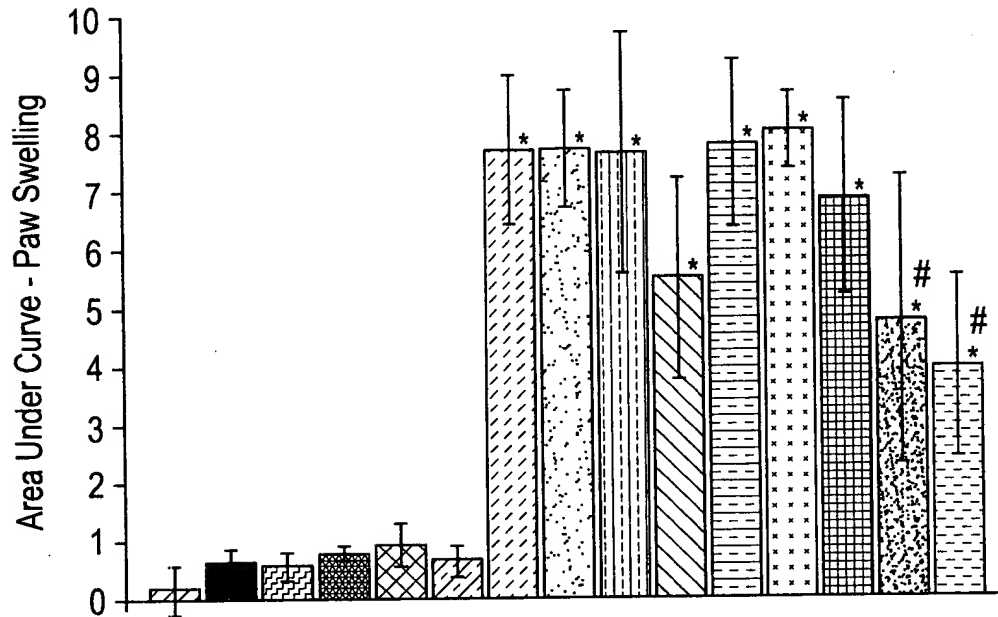
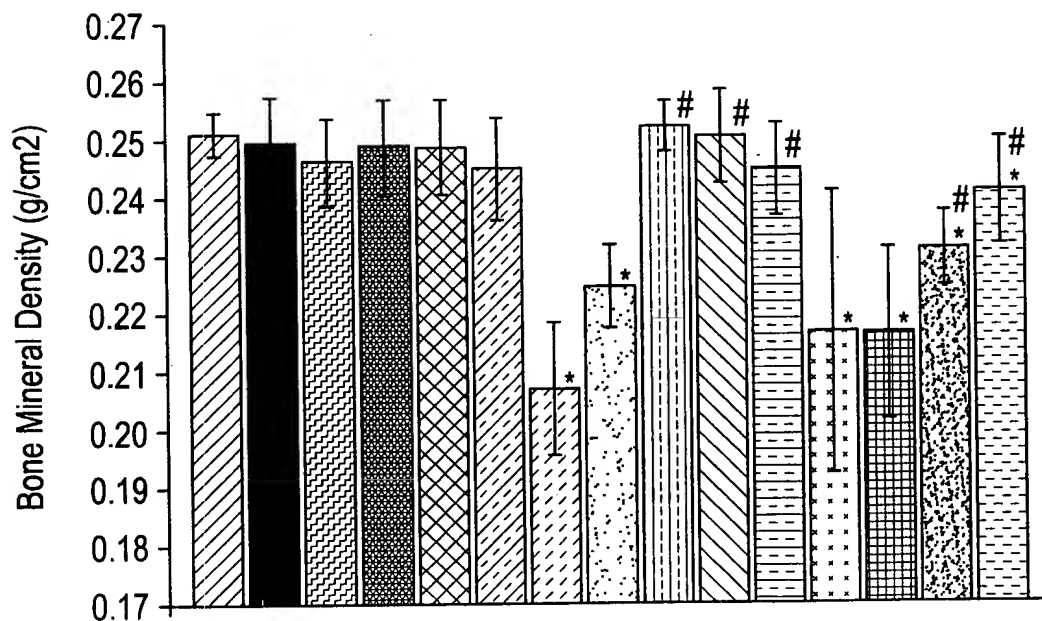


FIG. 30B-2



- |                                     |                                       |
|-------------------------------------|---------------------------------------|
| Normal                              | AdA + 1.0 mg/kg OPG-Fc (s.c.)         |
| Normal + 1.0 mg/kg OPG-Fc (s.c.)    | AdA + 0.25 mg/kg OPG-Fc (s.c.)        |
| Normal + 0.25 mg/kg OPG-Fc (s.c.)   | AdA + 0.0625 mg/kg OPG-Fc (s.c.)      |
| Normal + 0.0625 mg/kg OPG-Fc (s.c.) | AdA + 0.016 mg/kg OPG-Fc (s.c.)       |
| Normal + 0.016 mg/kg OPG-Fc (s.c.)  | AdA + 0.004 mg/kg OPG-Fc (s.c.)       |
| Normal + 0.004 mg/kg OPG-Fc (s.c.)  | AdA + 5.0 mg/kg/hr IL-1ra (2ML1)      |
| AdA control                         | AdA + 0.07 mg/kg Dexamethasone (s.c.) |

FIG. 31A

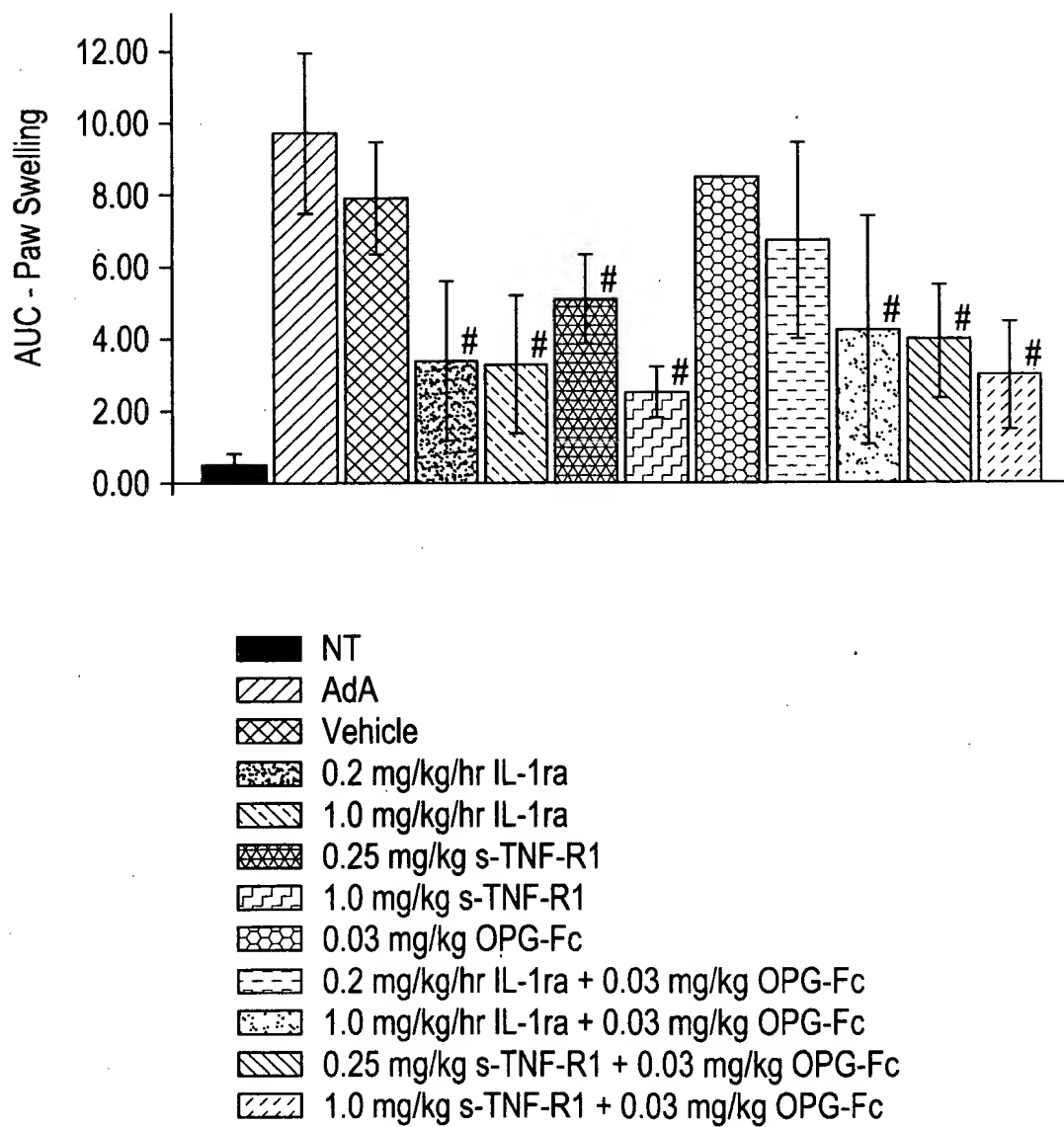


FIG. 31B

